MERCAPTANS/THIOLS COUNCIL
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December 4, 2001
Submitted electronically to:
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Christine Todd Whitman, Administrator
U.S. Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22116

Re: HPV Submission for Registration # – Methyl Mercaptans Analogs

Dear Ms. Whitman:

I am submitting the attached data package to EPA as part of the Mercaptans/Thiols Council (MTC) commitment under the U.S. High Production Volume (HPV) Challenge Program.

The attached data package was prepared for the Methyl Mercaptans analogs, which includes the following compounds:

CAS Numbers	Methyl Mercaptans
74-93-1	Methanethiol (Methyl Mercaptan)
5188-07-8	Methanethiol, sodium salt (Sodium Mercaptide)

This submission is being made on behalf of the following MTC member companies:

- Bayer Corporation
- ATOFINA Chemicals, Inc. (formerly Elf Atochem N.A., Inc.)
- Chevron Phillips Chemical Company LP (formerly Phillips Chemical Company)
- Natural Gas Odorizing, Inc., a wholly owned subsidiary of Occidental Chemical Corporation

If you have any questions, or would like to meet with MTC to discuss this submission, please do not hesitate to contact me at (703) 669-5688 or via e-mail at ehunt@va.adelphia.net.

Sincerely,

Submitted electronically

Elizabeth K. Hunt
Executive Director

Attachments:

- Methyl Mercaptan/Methyl Mercaptide Test Plan (MESHTESTPLAN12-01.doc)
- IUCLID Dossier for Methyl Mercaptan (IUCLID74-93-1.doc)
- IUCLID Dossier for Sodium Mercaptide (IUCLID5188-07-8.doc)
- IUCLID of Select Studies for Hydrogen Sulfide (IUCLID7783-06-4.doc)

Please note the change of address, phone, fax and e-mail for the Council.

AR201-13353A

Methyl Mercaptan (CAS 74-93-1)
Methyl Mercaptide (CAS 5188-07-8)

High Production Volume Challenge Program
Test Plan

Submitted By:

Mercaptans/Thiols Council
941 Rhonda Place S.E.
Leesburg, VA 20175
(703) 669-5688

Submission Date:
December 4, 2001

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I. PLAIN LANGUAGE SUMMARY

The Mercaptans/Thiols Council (MTC) has volunteered to provide basic hazard information for Methyl Mercaptan (MeSH), CAS Number 74-93-1, and Methyl Mercaptide (NaMeSH), CAS Number 5188-07-8, as part of the United States Environmental Protection Agency's High Production Volume Chemical Challenge Program (HPV Challenge).

MeSH and NaMeSH should be considered analogs because NaMeSH is the salt of MeSH. NaMeSH will be used for the proposed testing because it is converted to MeSH and it is safer and easier to handle.

In consideration of animal welfare concerns to minimize the use of animals in the testing of chemicals, the MTC has conducted a thorough literature search for all available data, published and unpublished. It has also performed an analysis of the adequacy of the existing data. In addition, we have used structure-activity relationship information to fill certain data gaps.

MeSH and NaMeSH have, or are expected to have, similar health and environmental hazard profiles. The metabolism and toxicological properties of hydrogen sulfide (H_2S) are similar to MeSH. For reproductive and developmental toxicity, surrogate data from a H_2S study is included.

Sufficient data are available to assess the physical/chemical and human health endpoints included in the HPV Challenge. Computer modeling or testing is proposed to better evaluate the environmental fate and aquatic toxicity of these chemicals. The following studies are being proposed to better assess the ecotoxicity and environmental fate of MeSH and NaMeSH: acute fish toxicity and acute algae inhibition. Computer modeling will be used to evaluate the photodegradation and transport in the environment (fugacity) for MeSH and NaMeSH.

CAS#	Name	Acronym	Status
74-93-1	Methyl Mercaptan	MeSH	Sponsored in HPV program
5188-07-8	Sodium Mercaptide	NaMeSH	Sponsored in HPV program
7783-06-4	Hydrogen Sulfide	H_2S	Not part of the HPV program but data to fill data gaps

II. MEMBER COMPANIES OF THE MERCAPTANS/THIOLS COUNCIL

- ATOFINA Chemicals, Inc (formerly Elf Atochem North America, Inc)
- Bayer Corporation*
- Chevron Phillips Chemical Company LP (formerly Phillips Chemical Company, Phillips Petroleum Company)
- Natural Gas Odorizing, Inc., a wholly owned subsidiary of Occidental Chemical Corporation*

* Members not producing/importing MeSH and NaMeSH

III. INTRODUCTION

The Mercaptans/Thiols Council (MTC) has volunteered to participate in the Environmental Protection Agency's High Production Volume Challenge Program (HPV Challenge) to assess the health and environmental hazards, including selected physical chemical characteristics of methyl mercaptan (MeSH) and methyl mercaptide (NaMeSH). These two chemicals should be considered analogs according to an EPA guidance document, 1999.

This document includes justification for considering MeSH and NaMeSH as analogs to be used interchangeably to assess the data endpoints included in the HPV Challenge. NaMeSH is the sodium salt of MeSH, which is formed when MeSH is added to a sodium hydroxide solution. NaMeSH is expected to be converted to MeSH because the pH values normally found in biological and environmental systems are below the pKa (10.7). Thus, toxicological information obtained for NaMeSH in these studies is equivalent to that of MeSH.

Our objective in this submission is to evaluate the available data and determine what additional data are needed to adequately characterize the human health and environmental hazards of MeSH and NaMeSH (Table 1). An evaluation of the available data for both MeSH and NaMeSH and proposed test plan are included. In addition, available information for hydrogen sulfide (H_2S) is included as surrogate data to complete a MeSH and NaMeSH health hazard assessment.

Based on our review of available data, MTC proposes to conduct acute fish toxicity and algae inhibition studies with NaMeSH. In addition, appropriate computer models will be used to calculate data for selected environmental fate and physical/chemical endpoints of MeSH and NaMeSH as suggested in EPA guidance documents. Substantial and scientifically defensible similarities between MeSH/NaMeSH and H_2S toxicological data provide the scientific basis to justify the use of reproductive and developmental H_2S toxicological information as surrogate data for MeSH and NaMeSH. Robust summaries of selected studies for MeSH and NaMeSH, as well as, the relevant robust summaries for H_2S are included in Appendices I, II and III.

TABLE 1: Matrix of Available Data and Proposed Data Development for Methyl Mercaptan (MeSH) and Methyl Mercaptide (NaMeSH)

EPA HPV Challenge Endpoint	Results of Data Review/Proposed Data Development
Physicochemical Properties	Calculate / Identify Existing Data
Biodegradation	Adequate Data / No Testing
Photodegradation	Calculation
Hydrolysis	Adequate Data/No Testing
Fugacity	Calculation
Acute Fish Toxicity	Testing Proposed
Acute Daphnia Toxicity	Adequate Data/ No Testing
Algae Toxicity	Testing Proposed
Acute Oral Toxicity	Adequate Data / No Testing
Acute Inhalation Toxicity	Adequate Data / No Testing
Acute Dermal Toxicity	Adequate Data / No Testing
Repeated Dose Toxicity	Adequate Data / No Testing
Genotoxicity, In Vitro	Adequate Data / No Testing
Genotoxicity, In Vivo	Adequate Data / No Testing
Reproductive/Developmental Toxicity	Adequate Data (H_2S data) / No testing

IV. USES OF METHYL MERCAPTAN AND METHYL MERCAPTIDE

Methyl mercaptan is used as a gas odorant, catalyst, intermediate in manufacturing jet fuels and in the synthesis of methionine, as well as, the manufacture of some pesticides and fungicides.

NaMeSH is an easier to handle, pumpable solution, which reduces the safety hazards of a toxic gas under pressure, associated with MeSH. Most applications for NaMeSH are for smaller reactions where the high value of the end product can justify the higher cost of using the more costly raw material. In all of these reactions, the MeSH moiety is released from the high pH solution by lowering the pH to be reacted with another chemical species, or is reacted directly from the NaMeSH.

V. ANALOG CHARACTERIZATION

According to the EPA, chemicals and their corresponding salts may be considered analogs (EPA guidance document, 1999). NaMeSH is the salt of MeSH and is produced by bubbling MeSH through aqueous sodium hydroxide. The value for the pK_a of NaMeSH in water at 25°C is 10.70 (Lange, 1985). At a temperature of 25°C and a pH of 10.7, there is an equilibrium of 50% MeSH and 50% NaMeSH dissolved in the water. The higher the pH, the more the equilibrium is shifted to the salt mercaptide

moiety. In other words, as a pH of 14 is approached, the solution moves toward being mostly NaMeSH. Conversely, the lower the pH, the more the equilibrium shifts to the pure MeSH being the chemical species in the aqueous phase.

For each drop in pH unit of 1.0, there is a corresponding drop by a factor of ten in the concentration of the NaMeSH in the aqueous state or conversely an increase in the MeSH. At a pH of 8.7, the ratio has been changed to roughly 1:100 (NaMeSH to MeSH), which means that the important chemical species present in solution is now the MeSH. The pH of a biological system is around 7.0 to 7.4 (CRC Handbook, 1995); therefore, the ratio of NaMeSH to MeSH is at least 1:1000. Thus, in biological systems, NaMeSH will be converted to MeSH.

Since all testing will be conducted below the pKa of NaMeSH, we propose that NaMeSH and MeSH be considered as analogs for assessing the health and environmental endpoints outlined in the HPV Challenge Program.

VI. EVALUATION OF PHYSICOCHEMICAL DATA

The physicochemical endpoints for the HPV Challenge include: melting point, boiling point, vapor pressure, water solubility, and octanol/water partition coefficient (K_{ow}). The physical/chemical data are detailed in the IUCLID dossiers (Appendices I and II). The data provided below are measured, reported in handbooks, or calculated using the EPIWIN© computer model. This model is discussed in the US EPA document entitled "The Use of Structure-Activity Relationships (SAR) in the High Production Volume Chemicals Challenge Program"(1999) and will be used to calculate physicochemical data for some of the endpoints where data are not available. The water solubility of NaMeSH will be confirmed in the aquatic toxicity studies proposed in Section VIII.

TABLE 2: Summary of Physical/Chemical Characteristics of MeSH and NaMeSH

	MeSH (gas)	NaMeSH (liquid)
CAS#	74-93-1	5188-07-8
Melting Point (°C)	-123	210 (crystallization temp 55)
Boiling Point (°C)	5.96 under 1 atm	69
Vapor Pressure (mm Hg@25°C)	1.51E+3	1.08E-6
Water solubility (mg/l)	23300	1000000
Octanol/Water Partition Coefficient (Kow)	0.78	-2.3

SUMMARY: No additional testing is proposed for purposes of the HPV Challenge Program.

VII. EVALUATION OF ENVIRONMENTAL FATE DATA AND PROPOSED TESTING

Environmental fate endpoints for the HPV Challenge include: biodegradation, photodegradation, hydrolysis, and fugacity. Robust summaries on available environmental fate data, prepared in accordance with criteria outlined in the HPV Challenge, are provided in Appendices I and II.

A. Biodegradation

Biodegradation data, available for both products in this category, show that these products are readily biodegradable. NaMeSH is readily biodegradable in an OECD 301d "Ready biodegradability: Closed bottle test" (Elf Atochem, 1995). The overwhelming data indicate MeSH is biodegradable (Appendix I). The available data are sufficient to assess the biodegradability of MeSH and NaMeSH.

SUMMARY: No additional testing is proposed for purposes of the HPV Challenge Program.

B. Photodegradation – Atmospheric Oxidation

Photodegradation can be measured (OECD test guideline 113) or estimated using models accepted by the US EPA and other authorities. An estimation method accepted by the US EPA includes the calculation of atmospheric oxidation potential (AOP). Atmospheric oxidation as a result of hydroxyl radical attack is not direct photochemical degradation, but rather indirect degradation. AOPs can be calculated using a computer model. The computer program AOPWIN (Atmospheric Oxidation Program for Microsoft Windows), used by the US EPA OPPTS (Office of Pollution Prevention and Toxic Substances), calculates a chemical half-life based on an overall OH^- reaction rate constant, a 12-hour day, and a given OH^- concentration. AOPWIN will be used to estimate photodegradation for MeSH and NaMeSH.

SUMMARY: Photodegradation estimates (AOPWIN model) are proposed for MeSH and NaMeSH.

C. Hydrolysis

Hydrolysis of an organic chemical is the transformation process in which a water molecule or hydroxide ion reacts to form a new carbon-oxygen bond. Chemicals that have a potential to hydrolyze include: alkyl halides, amides, carbamates, carboxylic acid esters and lactones, epoxides, phosphate esters, and sulfonic acid esters. Stability in water can be measured (OECD test guideline 111) or estimated using models (HYDROWIN) accepted by the US EPA and other authorities. HYDROWIN cannot estimate the hydrolysis for structures such as MeSH and NaMeSH. Measuring hydrolysis at the specific pHs cited in OECD 111 guideline would result in the conversion of NaMeSH to MeSH.

In addition, MeSH and NaMeSH do not contain hydrolyzable moieties. Analytical measurement of MeSH in the acute daphnia study indicates MeSH is stable. The available data are sufficient to assess the hydrolysis of MeSH and NaMeSH.

SUMMARY: No additional testing is proposed for purposes of the HPV Challenge Program.

D. Chemical Transport and Distribution In The Environment (Fugacity Modeling)

Chemical transport can be assessed using a Level III fugacity model to determine the relative distribution of chemicals between selected environmental compartments such as air, soil, sediment, and water. A widely used fugacity model is the Equilibrium Criterion Model that is included in the EPIWIN version 3.02 software currently used by EPA to evaluate new chemicals.

SUMMARY: An estimation from a Level III fugacity model is proposed to assess the transport and distribution of MeSH and NaMeSH in the environment.

VIII. EVALUATION OF ECOTOXICITY DATA AND PROPOSED TESTING

Aquatic toxicity endpoints for the HPV Challenge include: acute toxicity to freshwater fish, invertebrates, and freshwater algae. Based on the available data, MeSH and NaMeSH are expected to be toxic to aquatic organisms. For proposed testing, NaMesh will be used since it is safer and easier to handle and will convert to MeSH. Robust summaries on available ecotoxicology data, prepared in accordance with criteria outlined in the HPV Challenge, are provided in Appendices I and II.

A. Acute Fish Toxicity

In a 1952 study, MeSH is toxic to a variety of fish species with lethality occurring at concentrations between 0.5 – 1.75 ppm. Similar toxicity to fish is expected for NaMeSH. In order to adequately compare the data, an acute fish toxicity study (OECD 203) is proposed for NaMeSH.

SUMMARY: An acute fish toxicity study (OECD 203) with NaMeSH is proposed.

B. Acute Daphnia Toxicity

Based on a recent guideline (OECD 202 Part 1) study, NaMeSH is toxic to daphnia. The EC_{50} (concentration immobilizing 50 percent of daphnia) after 48-hour exposure was between 1.32 – 2.46 mg/l. In fact, MeSH was the measured moiety in this study providing further support for the use of NaMeSH data to assess MeSH aquatic hazards. Similar results are expected for MeSH.

Sufficient data are available to assess the hazards of MeSH and NaMeSH to daphnia.

SUMMARY: No additional testing is proposed for purposes of the HPV Challenge Program.

C. Acute Algae Inhibition

Available data indicate MeSH and NaMeSH are toxic to fish and invertebrates. However, no data are available to assess the effects of MeSH and NaMeSH on algae (often more sensitive to toxic insult than fish and daphnia). Therefore, an algae inhibition study (OECD guideline 201) is proposed for NaMeSH.

SUMMARY: An algal inhibition study (OECD 201) is proposed for NaMeSH.

IX. EVALUATION OF HEALTH EFFECTS DATA AND PROPOSED TESTING

The mammalian toxicity endpoints for the HPV Challenge Program include: acute toxicity, repeat dose toxicity, genetic toxicity (including point mutations and chromosomal effects), and reproductive/developmental toxicity. Robust summaries on available toxicology data, prepared in accordance with criteria outlined in the HPV Challenge Program guidance documents, are provided in Appendices I and II.

A. Acute Toxicity

Acute toxicity studies have been conducted on MeSH and NaMeSH, which are summarized in Table 3. Inhalation exposure was used to assess the acute toxicity for MeSH, and oral and dermal exposure were used to evaluate the acute toxicity of NaMeSH. Regardless of the route of exposure, the toxicity was similar with CNS and respiratory depression, the common symptoms noted after high dose acute exposure. The available data are sufficient to assess hazards from acute exposure to MeSH and NaMeSH.

TABLE 3: Acute Toxicity of MeSH and NaMeSH

	MeSH (gas)	NaMeSH (liquid)
Inhalation LC_{50} (ppm)	675[1]	No data
Oral LD_{50} (mg/kg)	NA	109[2]
Dermal LD_{50} (mg/kg)	NA	>84[3]

NA = not applicable
1 Tansy et al, 1981
2 Elf Atochem, 1989
3 Elf Atochem, 1994

SUMMARY: No additional testing is proposed for purposes of the HPV Challenge Program.

B. Repeat Dose Toxicity

A 90-day repeat dose inhalation toxicity study has been conducted on MeSH. Male Sprague-Dawley rats were exposed to 2, 17 and 57 ppm for 7 hr/day, 5-days/week. Terminal body weights, organ weights, oxygen consumption, systolic blood pressure, intestinal transit activities, SMA 12/60 Analysis[1], and histopathology of selected organs were evaluated. No mortality was observed in any of the sham or exposed population of rats. The high dose group had a statistically significant decrease in body weight gain. The authors state that although some average organ weights were significantly different from corresponding sham values, there were no obvious dose-related trends (Tansy et al, 1981).

According to the literature, mercaptans are known to be potent ocular and dermal irritants in workers at levels exceeding acceptable workplace exposure standards. The American Conference of Governmental Industrial Hygienists (ACGIH) recommends a threshold limit value (TLV), 8-hour time weighted average (TWA), of 0.5 ppm for MeSH (ACGIH, 2001). Due to the intense odor and irritation of MeSH and NaMeSH, workers would limit exposure to levels above the TLV. Sufficient data are available to assess the hazards associated with repeated exposure to MeSH and NaMeSH.

SUMMARY: No additional testing is proposed for purposes of the HPV Challenge Program.

C. Genetic Toxicity

1. Point Mutation

NaMeSH is not mutagenic in bacterial mutagenicity assays (Elf Atochem, 1992). The available data are sufficient to assess the mutagenic hazards of MeSH and NaMeSH.

SUMMARY: No additional testing is proposed for purposes of the HPV Challenge Program.

2. Chromosomal Aberrations

MeSH was negative in a mouse micronucleus assay (Elf Atochem, 1997). NaMeSH was negative in a mouse micronucleus assay (Elf Atochem, 1999). The available data are sufficient to assess the chromosomal effects of MeSH and NaMeSH.
SUMMARY: No additional testing is proposed for purposes of the HPV Challenge Program.

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[1] SMA 12/60 Analysis included 13 different blood serum components; total protein, albumin, Ca++, inorganic phosphorus, cholesterol, BUN, Uric acid, total bilirubin, alkaline phosphatase, LDH, SGPT, SGOT, glucose. No blood cell count analysis was performed.

D. Reproductive and Developmental Toxicity

No reproductive or developmental toxicity studies are available on MeSH or NaMeSH. Repeat dose studies conducted on MeSH did not evaluate the reproductive organs (Tansy et al, 1981).

A recent reproductive/developmental toxicity study of H_2S is included as surrogate data to assess the reproductive and developmental toxicity of MeSH and NaMeSH. Robust Summaries for select H2S studies are included in Appendix III.

1. Rationale for Using H_2S Data

a. Similar Physical/Chemical Characteristics

The physical properties provided in Table 4 support the argument that H_2S and MeSH are similar. NaMeSH, a liquid, is different from the other two gases; however, it is a liquid, salt analog of MeSH in biological systems.

TABLE 4: Comparison of Physical/Chemical Properties

Chemical Name	Hydrogen sulfide	Methyl Mercaptan	Methyl Mercaptide
Acronym	H_2S	MeSH	NaMeSH
CAS #	7783-06-4	74-93-1	5188-07-8
Chemical Structure	H – S – H	H | H – C – S - H | H	H | H – C – S - Na | H
Molecular Weight	34.08	48.11	70.08
Color	Colorless	Colorless	Colorless
Physical State	Gas	Gas	Liquid
Melting Point (°C)	-85.49	-123	-12
Boiling Point (°C)	-60.33	5.95	>210
Octanol/Water Partition Coefficient	0.96	0.78	-2.3
Density	1.539@0°C	0.8665@20°C	1.34@20°C
Odor	Rotten eggs	Rotten cabbage	Odorous
Odor threshold Water Air	 0.000029 ppm 0.0005 ppm	 0.000024 ppm 0.0016 ppm	 Not determined Not determined
Water solubility @ 25°C	4.31 g/l (@20°C)	15.39 g/l	Miscible
Vapor Pressure (mmHg @ 22°C)	14469	1520	1.08E-6 (25°C)
Explosive limit	4.3 – 46%	3.9 – 22%	Not determined

b. Similar Metabolism

H_2S Metabolism

The metabolism of H2S and MeSH appear to result in the same chemical species, sulfate (SO_4^{2-}). H_2S enters the circulation directly across the alveolar-capillary barrier, where it dissociates in part, into the active sulfide ion (HS^-). The most common route of exposure, and the one of most concern, is inhalation. The principle fate of absorbed H_2S following inhalation is oxidation to sulfates and excretion in the urine (Beauchamp et al, 1984). Most absorbed H_2S is oxidized by 15 hours following exposure (Kangas and Savolainen, 1987). Bartholomew et al. (1980) noted the primary location for these metabolic reactions was in the liver. H_2S can also be metabolized by methylation and reaction with metallo- or disulfide-containing proteins. However, the major route is oxidation of sulfide to sulfate (Beauchamp et al, 1984).

MeSH Metabolism

MeSH is a gas; therefore, the route of most concern is inhalation. The inhaled MeSH is rapidly absorbed and is readily oxidized to carbon dioxide and sulfate by splitting of the central carbon-sulfur bond. The primary end result is sulfate excreted in the urine (Blom et al, 1990).

Most of the MeSH metabolism work has been conducted following intraperitoneal (ip) injection (Derr and Draves, 1983;1984). These studies indicated that male Spague-Dawley rats eliminated 94% of the injected MeSH in the urine 21 hours after administration (Derr and Draves, 1983). MeSH is distributed in the plasma and in the blood cells (Al Mardini et al, 1988). Red blood cells are capable of oxidation of MeSH eventually to sulfate (SO_4^{2-}) and formate ($HCOO^-$) (Blom and Tangerman, 1988). The oxidation may also take place in the liver since MeSH is also a ligand for the mixed function oxidase (Dawson et al, 1983).

The 1990 Blom et al inhalation metabolism study with MeSH indicated that 80% of the administered MeSH was oxidized by red blood cells. Liver metabolism was not evaluated.

A recent study by Levitt et al. (1999) demonstrated that MeSH can be demethylated to H_2S, and further be converted to nonvolatile metabolites such as sulfate and thiosulfate in the cecal mucosa. Further studies by Furne et al. (2001) identified the same metabolic pathway for both H_2S and MeSH in other tissues including liver, plasma, and erythrocytes. Although cecal mucosa demonstrated a specialized function in metabolizing MeSH and H_2S, this data, as well as data obtained from other tissues demonstrate similar

metabolic profiles for MeSH and H_2S (Table 5, Figures 1 and1a). Mazel et al. (1964) described a microsomal enzyme system that may play an important role in demethylation of MeSH to H_2S.

TABLE 5: Averaged Percent of Sulfur-Containing Metabolites During Incubation of Various Rat Tissue Homogenates with H_2S or MeSH

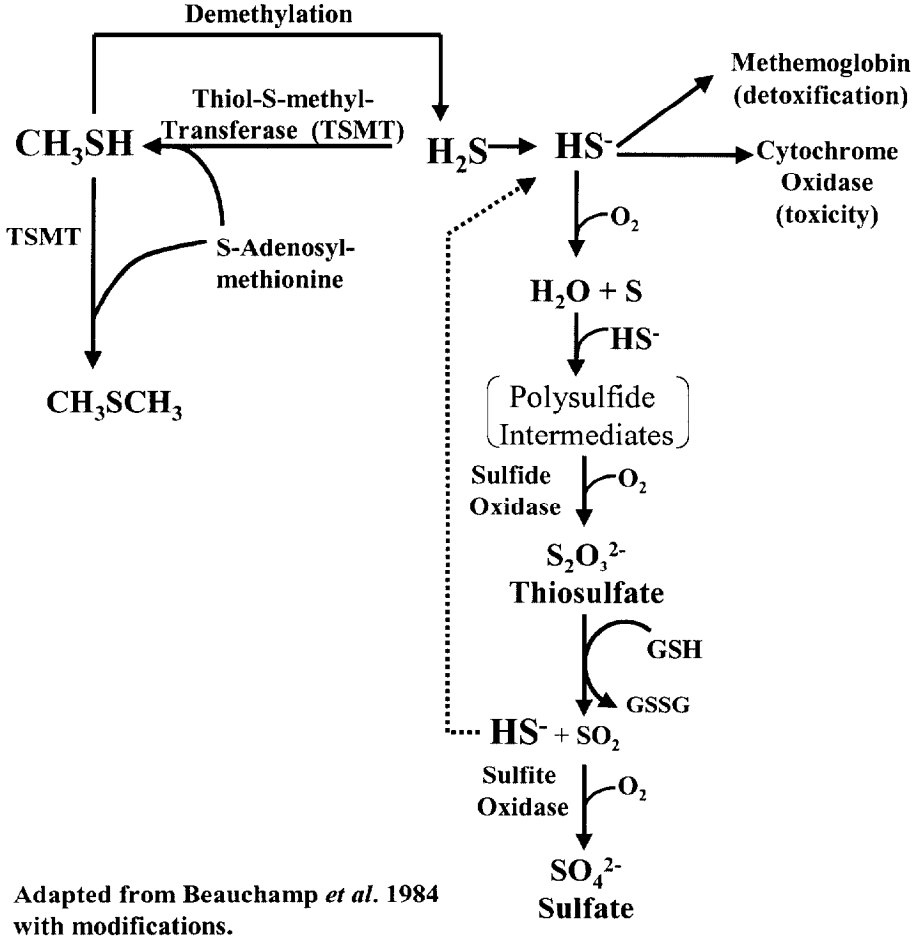
Tissue	H_2S			MeSH			
	$ThioSO_4$	SO_4	Total	$ThioSO_4$	SO_4	H_2S	Total
Liver	50	50	100	31	49	19	100
Muscle	60	40	100	31	52	<20*	100
Plasma	81	19	100	22	70	<20*	100
Erythrocytes	20	80	100	9	34	57	100

Adapted from Furne et al., 2001

Note: For muscle and plasma tissue treated with MeSH, levels of H_2S were below detection limits.

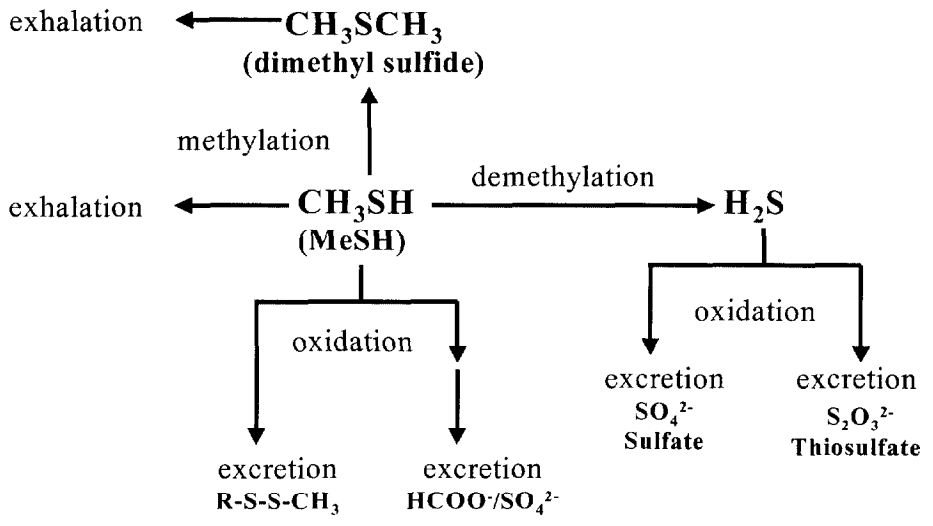
The exact pathway for MeSH metabolism has not been elucidated. It has strong similarities to H_2S in kinetics, primary route of elimination, and end product, sulfates (see Figures 1 and 1a).

FIGURE 1: Metabolic Scheme for H_2S



Adapted from Beauchamp *et al.* 1984 with modifications.

FIGURE 1a: Metabolic Schemes for MeSH



Adapted from Jappinen et al, 1993, with modifications

c. Similar Mechanism

The mechanism of toxicity of H_2S and MeSH is similar, i.e. cytochrome c oxidase inhibition. Waller (1977) reported that MeSH inhibits liver mitochondrial respiration by reacting with cytochrome c oxidase. This same mechanism of action has been reported for H_2S. Most investigators agree that MeSH acts like H_2S on the respiratory center, producing death by respiratory paralysis (Waller, 1977; Gosselin et al, 1984; Patty's, 1991). However, Wever indicated MeSH inhibitory activity for cytochrome c oxidase is much weaker than for H_2S (Wever et al, 1975). This indicates H_2S may be more toxic than MeSH.

d. Similar Acute Toxicity

The acute inhalation toxicity data summarized in Table 6 supports the statement that H_2S is more toxic than MeSH.

TABLE 6: Comparison of H_2S/MeSH/NaMeSH Toxicity Data

	H_2S (gas)	MeSH (gas)	NaMeSH (liquid)
Acute LC_{50} (ppm)	444[1]	675 [1]	No data
Subchronic NOAEL'S (ppm)	Fischer-344 rats –80[2] Sprague-Dawley Rats- 30ppm (females), 80 ppm (males)[3] $B6C3F_1$ Mice – 30[4]	57[1]	No data

1 Tansy et al, 1981
2 CIIT 1983a
3 CIIT 1983b
4 CIIT 1983c

Symptoms associated with acute MeSH exposure are similar to those of H_2S. Inhalation of MeSH can cause narcosis, headache, nausea, pulmonary irritation, and convulsions in humans. Exposure to high concentrations can result in respiratory paralysis and death (Hazardous Properties, 1999).

e. Similar Subchronic Toxicity

The subchronic toxicity data are similar for H_2S and MeSH as reflected in the No Observed Adverse Effect Levels (NOAELS) shown in Table 6. When animals were exposed for 90 days to either chemical, no treatment – related changes were detected by gross or histopathological examination of the gut, lung, heart, liver, kidneys, or other organs. Body weights and organ weights were the only endpoints of overlap for the two chemicals for the 90-day studies. The results of these endpoints are summarized below.

Subchronic H_2S Exposures:
No treatment-related body weight changes were noted in male or female Fischer-344 rats exposed to airborne concentrations of 10, 30 and 80 ppm of H_2S for 6 hr/day, 5 days/wk for 90 days (CIIT, 1983a). However, when Sprague-Dawley rats were exposed to the same regimen, females at 80 ppm showed a significant (10%) decrease in body weight at the end of the study compared to controls. At 80 ppm, the body weight of male Sprague-Dawley rats was significantly less (8%) than controls during weeks 1-3, but the final body weight differences were not significant (CIIT, 1983b). Similarly, B6C3F1 mice of both sexes exposed to 80 ppm, using the same testing regimen as above, showed a 7-14% decrease in body weight compared to controls (CIIT, 1983c).

Subchronic MeSH Exposures:
A 90-day repeat dose inhalation toxicity study has been conducted on MeSH. Male Sprague-Dawley rats were exposed to 2, 17, or 57 ppm MeSH for 7 hours/day, 5 days/week, for 90 days. Terminal body weights, organ weights, oxygen consumption, systolic blood pressure, intestinal transit activities and SMA 12/60 Analysis were evaluated. No mortality was observed in any of the sham or exposed population of rats. Average terminal body weights were lower in the exposed groups than those of sham controls for all rats. This difference was only statistically different at the 57 ppm exposure level, which showed a 15% decrease in terminal body weight. The authors state that although some average organ weights were significantly different from corresponding sham values, there were no obvious dose-related trends (Tansy et al, 1981).

Statistically, significant changes were observed in serum components of blood samples from animals of all exposed groups. However, none of these trends were dose-related at the 95% confidence level. The H_2S study evaluated blood cell parameters, but did not evaluate serum components.

f. Conclusion of Data Comparison

In conclusion, the data presented for MeSH and H_2S indicates they have similar physical/chemical characteristics, similar metabolic profiles, similar mechanism, and similar toxicity following acute and subchronic exposure. The toxicity of H_2S is slightly greater than MeSH as judged by several authors (Tansy et al, 1981; Patty's 1991). This may be due to the higher affinity H_2S has for the cytochrome c oxidase enzyme than does MeSH as explained by Wever (1975). Based on this information, the use of the H_2S data to fill the Reproductive/Developmental data gap should be accepted as a worse case scenario.

2. H_2S Reproductive/Developmental Neurotoxicity Study

In 2000, Dorman et al., published a reproduction/developmental toxicity study with H2S. This study was conducted using the OECD 421 guideline and included a neurodevelopmental component. Briefly, Sprague-Dawley rats were exposed via inhalation to concentrations of H_2S up to 80 ppm. The data from this study indicate H_2S does not cause adverse effects on reproductive endpoints, or on developmental endpoints including: pinnae detachment, incisor eruption, negative geotaxis, eyelid separation, vaginal patency, or balano-preputial separation. In addition, no effects were observed in motor activity, passive avoidance, functional observation battery, acoustic startle response or neuropathology (including gross and histological brain pathology). In conclusion, this study indicated that H_2S

is neither a reproductive toxicant, teratogen nor a behavioral developmental neurotoxicant in the rat at levels significantly higher than occupationally relevant exposure concentrations (e.g. 10 ppm TWA, ACGIH).

The available data are sufficient to assess the reproductive/ developmental hazard of MeSH and NaMeSH.

SUMMARY: No additional testing is proposed for purposes of the HPV Challenge Program.

Additional Concern: MeSH is highly odorous (odor threshold 1.6 ppb). Therefore, it has excellent warning properties. People do not willingly or unknowingly expose themselves to this chemical at concentrations greater than 1-10 ppm. The odor does preclude testing MeSH at high concentrations because communities surrounding the contract laboratories complain about the nuisance odor.

X. CONCLUSIONS

Sufficient data to evaluate several of the endpoints listed in the HPV Challenge are available for MeSH and NaMeSH as summarized in Table 7.

Physical/chemical characteristics (melting point, boiling point, vapor pressure, and water solubility) are available or can be calculated for MeSH and NaMeSH.

To evaluate environmental fate, data are available or can be calculated using EPA approved models for photodegradation and fugacity (transport and distribution in the environment).

NaMeSH is toxic to daphnia, similar results are expected for MeSH. No adequate data are available to assess the toxicity to fish and alga. Therefore, acute fish toxicity and algae inhibition studies are proposed for NaMeSH.

Mammalian toxicology data on MeSH and NaMeSH have shown central nervous system effects following acute exposure to high doses. Adequate data are available indicating MeSH and NaMeSH are not genotoxic. Since MeSH and NaMeSH are similar to H_2S, adverse effects to the reproductive system or developing fetus are not anticipated. Repeated exposure to MeSH and NaMeSH is not expected to cause adverse effects based on the results from a 90-day inhalation study with MeSH.

SUMMARY: EPIWIN software is proposed to estimate photodegradation and fugacity for MeSH and NaMeSH. In addition, acute fish toxicity and algae inhibition studies are proposed with NaMeSH.

TABLE 7: Matrix of Available Data for MeSH and NaMeSH by OECD SIDS Endpoints

OECD SIDS Endpoints	Methyl Mercaptan (MeSH)	Methyl Mercaptide (NaMeSH)
Physicochemical		
Melting point	Data available	Data available
Boiling point	Data available	Data available
Vapor Pressure	Data available	Data available
Water Solubility	Data available	Data available
Octanol/Water Partition Coefficient	Data available	Data available
Environmental Fate		
Biodegradation	Data available	Data available
Photodegradation	Calculated	Calculated
Hydrolysis	NA based on chemical properties	NA
Fugacity	Calculated	Calculated
Aquatic Toxicity		
Algae	RA	Testing Proposed
Invertebrate	RA	Data available
Fish	RA	Testing Proposed
Acute Mammalian Toxicity		
Oral	N/A based on chemical properties	Data available
Inhalation	Data available	NA
Dermal	NA	Data available
Repeated Dose Toxicity		
Inhalation	Data available	RA
Genetic Toxicity		
Point Mutation	RA	Data available
Chromosomal Effects	Data available	Data available
Reproductive Toxicity		
Inhalation	RA – H_2S	RA – H_2S
Developmental Toxicity		
Inhalation	RA – H_2S	RA – H_2S

Key:
NA – Not Applicable
RA – Read Across From Existing Data or From Proposed Testing

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IUCLID

Data Set

Existing Chemical	:	ID: 74-93-1
CAS No.	:	74-93-1
EINECS Name	:	methanethiol
EC No.	:	200-822-1
TSCA Name	:	Methanethiol
Molecular Formula	:	CH4S

Producer related part

Company	:	Atofina
Creation date	:	05.08.1999

Substance related part

Company	:	Atofina
Creation date	:	05.08.1999
Status	:	
Memo	:	
Printing date	:	26.10.2001
Revision date	:	
Date of last update	:	26.10.2001
Number of pages	:	35
Chapter (profile)	:	Chapter: 2, 3, 4, 5
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

2.1 MELTING POINT

Value	:	= -123 °C
Sublimation	:	
Method	:	other: no data
Year	:	
GLP	:	no data
Test substance	:	no data
Source	:	Atofina, Paris-la-Défense, France.
Reliability	:	(2) valid with restrictions Data from Handbook
Flag	:	Critical study for SIDS endpoint
26.10.2001		(1) (2) (3)

2.2 BOILING POINT

Value	:	= 6 °C at 1033 hPa
Decomposition	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	no data
Source	:	Atofina, Paris-la-Défense, France.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint
26.10.2001		(1) (4) (5)

2.3 DENSITY

Type	:	density
Value	:	at °C
Method	:	
Year	:	
GLP	:	
Test substance	:	no data

Remark :

Temperature (°C)	Pression (bar)	Liquide (kg/m3)(***)	Vapeur (kg/m3)
0(*)	0.80	894(**)	1.73
15(*)	1.38	874(**)	2.96
50(*)	4.26	827	8.13

(*) : liquid/vapor equilibrium
(**): extrapolated values
(***): calculated values (from Air Liquide)

Source	:	Atofina, Paris-la-Défense, France.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint
26.10.2001		(1)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value	:	= 1650 hPa at 20 °C
Decomposition	:	
Method	:	other (measured)
Year	:	
GLP	:	no data
Test substance	:	no data
Source	:	Atofina, Paris-la-Défense, France.
Reliability	:	(2) valid with restrictions Data from Handbook
Flag	:	Critical study for SIDS endpoint
26.10.2001		(6) (7) (5)

Value	:	= 4400 hPa at 50 °C
Decomposition	:	
Method	:	other (measured)
Year	:	
GLP	:	no data
Test substance	:	no data
Source	:	Atofina, Paris-la-Défense, France.
Reliability	:	(2) valid with restrictions Data from Handbook
Flag	:	Critical study for SIDS endpoint
26.10.2001		(6) (7) (5)

Value	:	= 9500 hPa at 80 °C
Decomposition	:	
Method	:	other (measured)
Year	:	
GLP	:	no data
Test substance	:	no data
Source	:	Atofina, Paris-la-Défense, France.
Reliability	:	(2) valid with restrictions Data from Handbook
Flag	:	Critical study for SIDS endpoint
26.10.2001		(6) (7) (5)

2.5 PARTITION COEFFICIENT

Partition coefficient	:	octanol-water
Log pow	:	= .78 at °C
pH value	:	
Method	:	other (calculated)
Year	:	
GLP	:	no data
Test substance	:	no data
Remark	:	KowWin (LogKow) Log P Calculation
Source	:	Atofina, Paris-la-Défense, France.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

26.10.2001 (8)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	= 23.3 g/l at 20 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other: no data
Year	:	
GLP	:	no data
Test substance	:	no data
Source	:	Atofina, Paris la Défense
Reliability	:	(2) valid with restrictions Data from Handbook
Flag	:	Critical study for SIDS endpoint

26.10.2001 (9)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value	:	< -18 °C
Type	:	closed cup
Method	:	
Year	:	
GLP	:	no data
Test substance	:	
Source	:	Elf Aquitaine Lacq ECB - Existing Chemicals Ispra (VA)
Reliability	:	(4) not assignable

28.06.2001 (10)

2.8 AUTO FLAMMABILITY

Value	:	= 374 °C at
Method	:	
Year	:	
GLP	:	no data
Test substance	:	
Source	:	Elf Aquitaine Lacq ECB - Existing Chemicals Ispra (VA)
Reliability	:	(4) not assignable

28.06.2001 (10)

2.9 FLAMMABILITY

Result	:	flammable
Method	:	
Year	:	
GLP	:	no data
Test substance	:	
Remark	:	Thermal decomposition in sulfur anhydride, carbon monoxyde and carbon dioxyde
Source	:	Elf Aquitaine Lacq ECB - Existing Chemicals Ispra (VA)
Reliability	:	(4) not assignable

26.10.2001 (10)

2.10 EXPLOSIVE PROPERTIES

Method	:	
Year	:	
GLP	:	no data
Test substance	:	no data
Remark	:	Explosive limits: 3.9 to 21.8 %v/v in air
Source	:	Elf Aquitaine Lacq ECB - Existing Chemicals Ispra (VA)
Reliability	:	(4) not assignable

26.10.2001 (10)

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

Remark	:	Critical pressure: 71 000 hPa Critical temperature: 196.8 degree °C
Source	:	Elf Aquitaine Lacq ECB - Existing Chemicals Ispra (VA)
Reliability	:	(4) not assignable

28.09.2001 (10)

Remark	:	Henry's Law Constant: 3.13E-3 atm m3/mole (calculated) 0.123 (measured)
Source	:	Elf Aquitaine Lacq ECB - Existing Chemicals Ispra (VA)

23.10.1995 (11)

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	O3
Conc. of sensitizer	:	
Rate constant	:	cm^3/(molecule*sec)
Degradation	:	% after
Result	:	Second order rate constant: 0.00488/ppm/h Half-life time: 140 hours. Air mixture of the test compound was relatively unreactive . The introduction of sunlight enhanced decay rate in comparison to rate observed in the dark.
Source	:	Elf Aquitaine Lacq ECB - Existing Chemicals Ispra (VA)
Test condition	:	Initial O3 concentration : 0.10 ppm Initial compound concentration : 7.71 ppmv Tests were performed in Teflon bag reactors (125 l) filled with clean air.

23.10.1995 (12)

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	
Rate constant	:	= .0000000000256 cm^3/(molecule*sec)
Degradation	:	= 50 % after 46 minute(s)
Deg. product	:	
Method	:	other (measured)
Year	:	
GLP	:	
Test substance	:	
Source	:	Elf Aquitaine Lacq ECB - Existing Chemicals Ispra (VA)
Test condition	:	Method: flash photolysis-resonance fluorescence. OH radicals are produced by H-atom titration with large excess NO2.H atoms were generated by electrodeless microwave discharge of a small amount oh H2 introduced into the He carrier gas. Test compound concentration:(1.3-9.7)E12 molecules cm-3.

23.10.1995 (13)

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	500000 molecule/cm^3
Rate constant	:	= .0000000000329 cm^3/(molecule*sec)
Degradation	:	= 50 % after .5 day(s)
Deg. product	:	

Method	:	other (calculated)
Year	:	
GLP	:	
Test substance	:	
Source	:	Elf Aquitaine Lacq ECB - Existing Chemicals Ispra (VA)

23.10.1995 (14)

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	
Rate constant	:	cm^3/(molecule*sec)
Degradation	:	% after
Result	:	Photooxydation of methanethiol was performed with alkyl nitrites as sources of OH radicals. The main products of the reaction were SO2, CH3SO3H, H2SO4, with the final yields of 29, 40 and >= 2%, respectively. Degradation was 100% after 4 minutes.
Source	:	Elf Aquitaine Lacq ECB - Existing Chemicals Ispra (VA)
Test condition	:	Mixtures of olefin-NO-CH3SH were irradiated. The light source was six black-light lamps or xenon lamps. Analysis were performed by GC/MS and IR.

23.10.1995 (15)

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	
Rate constant	:	cm^3/(molecule*sec)
Degradation	:	% after
Remark	:	OH radicals were generated by the photolysis at 350 nm of 5 ppm of nitrous acid (HONO) in synthetic air at 1 atm pressure and room temperature. Rate constant : 0.904E-10 cm3 moleculeE-1 sE-1. Rate constant value is higher than measured directly using the resonance fluorescence technique at low total pressure. It is concluded that the reaction of OH with CH3SH is enhanced at high pressure. SO2 was the major product of reaction.
Source	:	Elf Aquitaine Lacq ECB - Existing Chemicals Ispra (VA)

23.10.1995 (16)

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	other: NOx
Conc. of sensitizer	:	
Rate constant	:	cm^3/(molecule*sec)
Degradation	:	% after

Result	:	8.7 ppm test compound was exposed in bag filled with clean air, to 1.7 ppm NO and 0.5 ppm NO2 to sunlight during 2 hours. Concentrations of test compound, SO2 and O3 produced were measured with GS-FID, ozone analyser and pulsed fluorescent SO2 analyser. Half-life with NOx was 2 hours.The test compound was 85% degraded after 5 hours (Ref 1). The reaction products included formaldehyde , SO2, methyl nitrate as well as methane sulfonic acid and inorganic sulfate (Ref 2).
Source	:	Elf Aquitaine Lacq ECB - Existing Chemicals Ispra (VA)

23.10.1995 (17)

3.1.2 STABILITY IN WATER

3.1.3 STABILITY IN SOIL

Type	:	laboratory
Radiolabel	:	no
Concentration	:	100 ppm
Soil temperature	:	23 °C
Soil humidity	:	
Soil classification	:	
Year	:	
Content of clay	:	= 5 - 72 %
Content of silt	:	%
Content of sand	:	= 2 - 93 %
Organic carbon	:	= .5 - 9.4 %
pH	:	= 4.8 - 7.7
Cation exch. capacity	:	
Microbial biomass	:	
Deg. product	:	
Method	:	
Year	:	1973
GLP	:	no
Test substance	:	no data
Result	:	Times required for 95% sorption of methyl mercaptan by soils from air initially containing 100 ppm (v/v) gas: - from 2 to 84 minutes for air-dry soils - from 12 to 130 minutes for moist soils (50% of water-holding capacity) Capacities of soils for sorption of methyl mercaptan: - from 2.4 to 32.1 mg of gas/g of soil for air-dry soils - from 2.2 to 21.4 mg of gas/g of soil for moist soils Experiments with steam-sterilized soils indicated that soil microorganisms play little part in the sorption of sulfur gases. It is concluded that soil has a potential for purification of industrial emissions polluted by sulfur gases.
Source	:	Elf Aquitaine Lacq ECB - Existing Chemicals Ispra (VA)
Test condition	:	The soils used were surface (0-15 cm) samples selected so that they differed in pH (4.8-7.7), organic-matter content (0.47-9.38% organic C) and texture (2-93% sand, 5-72% clay). Each sample was air-dried and crushed to pass a 2 mm screen.

The reaction vessels used to study gas sorption by soils were 65 ml narrow-mouth, screw-cap bottles sealed with valve caps.
Gas samples were injected and removed by gas syringes.

5 ml of methyl mercaptan were injected into sealed bottle containing 1 g of air-dry soil .
The gas concentration in the air of the bottle was equivalent to 100 ppm (v/v).
The rate of gas sorption was study by analysing by gas chromatography, samples (100 µl) of the air in the bottle.

All experiments were performed at 23°C.

The effects of soil sterilization on gas sorption were studied with soil samples heated in an autoclave at 121°C for 60 minutes.

28.09.2001 (18)

3.2.1 MONITORING DATA

Type of measurement :
Media : other
Concentration :
Method :

Result : Blue-green algal mats incubated anaerobically rapidly produce large amounts of volatile sulfur compounds, including hydrogen sulfide, methyl mercatan and dimethyl sulfide.
The major organic compound is methyl mercaptan.
Light inhibited production of volatile sulfur compounds, apparently because the algae then produced O2 rendering the system aerobic.
Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)
Test condition : Cores of algal mat collected from a hot spring effluent in Yellowstone National park were placed under anaerobic conditions in spring water in serum vials.The vials were incubated at in situ temperature in the dark.

23.10.1995 (19)

Type of measurement :
Media : air
Concentration :
Method :

Remark : Rate of emission of a biogenic sulfur gas : methyl mercaptan was measured in a variety of marine and freshwater wetlands habitats in the Florida everglades .
Results of emission rate were given in nmol/m2/h:
- Marine subtropical wetlands: 8 - 54
- Marine temperate wetlands: 5-300
- Freshwater subtropical wetlands: 1.7-8
- Freshwater temperate wetlands: 0-5

Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

23.10.1995 (20)

Type of measurement :
Media : surface water
Concentration :
Method :

Remark : Measurements of sulfur compounds in surface waters have been carried

out from a helicopter in the seas surrounding Scandinavia.
- Baltic sea: 5.0 ng S/l
- Kattegat/Skagerrak: 7.6 ng S/l
- North sea: 11 ng S/l

Calculated fluxes (µg S/m2/d) are respectively:
- Baltic sea: 4.4-6.7
- Kattegat/Skagerrak: 11-42
- North sea: 17-90

Methyl mercaptan contribute about 10% of the total flux of reduced sulfur , estimated to be 120-170 µg S/m2/d.

Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

23.10.1995 (21)

Type of measurement :
Media : surface water
Concentration :
Method :

Remark : Identities, concentrations and fluxes of volatile sulfur compounds were determined in 11 lakes in northwestern Ontario.Depth profiles showed accumulation below the mixed layer of methane thiol.
Range of values of methyl mercaptan were reported to be:
ND(not detected)-38 nM , mean values being 0.018-13 nM.
Accumulation rate of methyl mercaptan was 0.81 and 0.98 mmol/m2/d at a depth of 10m.

Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

23.10.1995 (22)

Type of measurement :
Media : other: anoxic water layers
Concentration :
Method :

Remark : Methane thiol and other volatile thio compounds have been determinad in a stratified lake (Schleinsee, SW Germany) which develops an anoxic hypolimnion every year during summer stratification.
Lakewater samples were taken in the middle of the lake where the maximum depth was 10.5 m.
The most abundant volatil organic sulfur compound was methane thiol.The highest concentration observed was 3 µg/l.

Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

23.10.1995 (23)

Type of measurement :
Media : other: sediment porewater
Concentration :
Method :

Remark : Seasonal variation of methane thiol concentrations in sediment porewater was determined in a danish estuary.
Significant methane thiol accumulation of up to 1 µM was found only in the deep, CH4-rich sediment below the SO42-zone (20 cm depth in summer).MSH was absent from the surface to about 25 cm depth in the winter and to about 5 cm in the summer.

Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

23.10.1995 (24)

Type of measurement :
Media : other: algae
Concentration :
Method :

Remark : Concentration of methyl mercaptan in culture of:
- Synechoccus cedrorum: 147+-43.2 ng/l
- Plectonema boryanum: 30+-16. ng/l.

Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

23.10.1995 (25)

Type of measurement :
Media : other: vegetation zones
Concentration :
Method :

Remark : Emission of methane thiol were measured within or across vegetation zones in a New Hampshire salt marsh.
Fluxes of MeSH were relatively constant for short time periods, highest from sites that contain the most biomass, highest during daylight hours. Rates of MeSH emissions were 100-150 nmol/m2/h during august 1987 and 80 nmol/m2/h during 1988 in a region where the vegetation dominant species was Spartina alterniflora.

Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

23.10.1995 (26)

Type of measurement :
Media : air
Concentration :
Method :

Remark : Emission gases was studied, from several processes: cooking of raw bone, concentrating of glue, refining of fat, and drying of bone. In results of the measurement of sulfur-containing odorants, it was found methyl mercaptan at the following levels:
- cooking plant: 804-1030 µl/l
- drying plant: <0.0002-0.0009 µl/l
- glue-concentrating plant: 0.021-0.048 µl/l
- fat-refining plant: 1.3-1.4 µl/l

Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

23.10.1995 (27)

Type of measurement :
Media : air
Concentration :
Method :

Remark : Field tests were performed in a pulp factory, in a municipal sewage plant and in the vicinity of an aeration basin, an aerobic basin and a sludge press of the wastewater treatment plant of a sulfite pulp factory.
- Sewage plant: 0.09 (pretreatment)-0.36 (sludge treatment) cm3/m3
- Sulfate pulp mill: 0.03 cm3/m3

Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

23.10.1995 (28)

Type of measurement :
Media : air

Concentration :
Method :

Remark : Methyl mercaptan was analyzed in the atmosphere of 16 finnish municipal wastewater treatmant plants and 18 pumping stations.
The average concentrations of methyl mercaptan was ranging from <0.10 to 0.69 µg/l.
Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

23.10.1995 (29)

Type of measurement :
Media : air
Concentration :
Method :

Remark : Volatile sulfur compounds in the atmosphere of a sewage system of the city of Hamburg was analyzed.
It was found in the range 0.1-3.4 ppm.
Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

23.10.1995 (30)

Type of measurement :
Media : air
Concentration :
Method :

Remark : An hygienic survey for sulfur compouns in kraft mills and in sulfite mills revealed concentrations varying from 0 to 15 ppm methyl mercaptan.
Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

23.10.1995 (31)

Type of measurement :
Media : air
Concentration :
Method :

Remark : Concentrations of gas contaminants in work area of kraft mills in British Columbia were measured.
It was found concentrations ranging from <0.01 to 1.5 ppm, with maximum of 7.3 ppm.
Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

23.10.1995 (32)

Type of measurement :
Media : air
Concentration :
Method :

Remark : Field study was performed in eastern United States in order to determine flux of sulfur gases from a variety of soils.
Concerning methyl mercaptan, it was found a flux of 6.56 g S/m2/yr.
Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

23.10.1995 (33)

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

3.3.2 DISTRIBUTION

Media	:	water - air
Method	:	other (calculation)
Year	:	
Remark	:	A half-life of 2.2 hr for volatilization from a model river 1 m deep with a 1 m/sec current and 3 m/sec wind speed was calculated.

28.09.2001 (34)

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	Thiobacillus sp. (Bacteria)
Deg. product	:	
Method	:	
Year	:	1989
GLP	:	
Test substance	:	other TS: obtained from Seitetsu Chemical Industries Ltd. (Japan)
Result	:	Cells of Thiobacillus thioparus TK-m were immobilized on cylindrical porous polypropylene pellets, which were packed in an acrylic cylinder of 50 mm diameter up to the eight of 800 mm. 96% of a loading charge of 8.74 mmol/l/d methyl mercaptan were degraded after 26 d, at 21°C. The inlet concentration was 17.8 µl/l.
Source	:	Atofina, Paris-la-Défense, France.

18.09.2001 (35)

Type	:	aerobic
Inoculum	:	other: Hyphomicrobacterium EG
Deg. product	:	
Method	:	
Year	:	1984
GLP	:	
Test substance	:	no data
Remark	:	A sample from a biofilter used to aerobically treat dimethyl sulfide containing wastewater from a paper mill proved to be a suitable inoculum, allowing the enrichment in an aerobic chemostat of a stable community able to grow on DMSO.This community could oxidize DMSO, dimethyl sulfide and other compounds, such as methyl mercaptan which are believed to be intermediates in the pathway of dimethyl sulfide metabolism.The dominant organism of this community is a Hyphomicrobium sp. The rate of oxygen uptake by a mixed culture grown on DMSO , on methyl mercaptan as substrate at a concentration of 0.14 mM, was 6.7 mmol oxygen/h/g dry weight.
Source	:	Atofina, Paris-la-Défense, France.

28.09.2001 (36)

Type	:	anaerobic
Inoculum	:	other: anoxic aquatic sediments
Deg. product	:	
Method	:	
Year	:	1986
GLP	:	
Test substance	:	other TS: Purity: 96%; Matheson Scientific Inc.
Remark	:	Addition of 1 mM methyl mercaptan to Mono Lake sediments stimulated methanogenesis after the endogenous production ceased.Stimulation by methyl mercaptan was about 3.5 fold. Results are expressed in % stimulation (or inhibition) of methanogenesis: (µmoles of CH4 formed - endogenous µmole CH4 formed)/endogenous µmoles CH4 formed * 100. At concentration of methyl mercaptan from 20 to 52 µmole per bottle, % stimulation was 352 for Mono Lake, 7638 for Flax Pond, 174 for San Francisco bay. Methanogenesis was inibited in pelagic sediments of Big Soda Lake (% inhibition = - 7). It was also shown that production of methane was blocked by 2-bromoethanesulfonic acid and that sulfate did not influence the metabolism of millimolar level of methyl mercaptan added to sediments.
Source	:	Atofina, Paris-la-Défense, France.
Test condition	:	Sediment types: two estuarine salt marshes, a freshwater lake and two hypersaline, alkaline lakes. Anaerobic procedures were used for the preparation of the slurries, dispensed into serum bottles under N2. Selected bottles received substrate addition of Sulfur compounds.Bottles were incubated in the dark at 22°C with constant shaking (300 rpm).Incubation time lasted for 3 to 6 weeks.Methane in the headspace of the bottle was analyzed by gas chromatography.

28.09.2001 (37)

Type	:	anaerobic
Inoculum	:	other: methanogenic bacteria
Deg. product	:	
Method	:	
Year	:	1978
GLP	:	
Test substance	:	other TS: 14C-labelled MeSH (New England Nuclear)
Remark	:	MeSH was rapidly metabolized by methanogenic bacteria to methane and CO2: 40% CH4 and 12% CO2 after 8 hours. Anaerobic sewage digester sludge, also tested , was found to produce almost exclusively CH4, most likely because of the large concentrations of hydrogen donors in the digester sludge. Optimal temperature was found to be 37°C. Inhibition of this activity by chloroform suggested the involvement of methanogenic bacteria.
Source	:	Atofina, Paris-la-Défense, France.
Test condition	:	Five µl 1M NaOH containing 2.2 nmol 14C-labelled MeSH, as the sodium mercaptide were mixed with 5 µl 1 M HCl . This mixture was immediatly injected into a 10 ml serum vial containing 1 ml lake sediment (lake Mendota, Wisconsin) in a nitrogen atmosphere.

28.09.2001 (38)

Type	:	anaerobic
Inoculum	:	
Deg. product	:	
Method	:	
Year	:	1985
GLP	:	
Test substance	:	no data

Remark	:	In this investigation, the capability and performance of anaerobic biological decomposition of malodorous compounds (dimethyl sulfide, dimethyl disulfide, methyl mercaptan, H2S) in kraft pulping waste stream drains were studied. The results obtained showed that the sulfur containing mamodorous compounds can be removed by anaerobic digestion system, combined with an alkaline scrubbing process of digester gas. Only about 10% of methyl mercaptan was decomposed to H2S.
Source	:	Atofina, Paris-la-Défense, France.
Test condition	:	Inoculum was a thermophilic sludge acclimatized to a synthetic substrate containing methanol as main organic component.The dominant methanogenic bacteria were Methanosarcina. The conditions of temperature of 50°C and pH of 6.5 were the most suitable.

28.09.2001 (39)

Deg. product	:	
Method	:	
Year	:	1987
GLP	:	
Test substance	:	no data
Result	:	It was shown that methylmercaptan resulted in negligible corrosion of the concrete. At a pH of 8.5+-0.5, there was 0% loss of substance (measured by weighing the cubes of the test blocks) after 9 monts. The mean n°. of cells /cm2 of the Thiobacilli was <10. The Thiobacilli could not grow with methylmercaptan.In the 2 experiments, neither sulfuric acid nor sulfur was detectable on the concrete test blocks.
Source	:	Atofina, Paris-la-Défense, France.
Test condition	:	Pure cultures of Thiobacillus intermedius, Thiobacillus novellus, Thiobacillus neapolinatus and Thiobacillus thiooxidans were mixed.The mixture contained a total of 10e13 cells. It was sprayed as an aerosol on the surface of the concrete test blocks, in a special apparatus. The experiments were run at 30°C and a relative humidity of more than 95%. The experiments were made during from 9 to 12 months. In two experiments, the gas methylmercaptan was used at concentrations of 22+-4 and 2+-1 mg/m3.

18.09.2001 (40)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

Memo	:	Henry's Law Constant : 0.003124 atm-m3/mole (316.46 Pa m3/mole) at 25°C
Remark	:	Estimated

28.09.2001 (41)

Memo	:	pKa Dissociation Constant : 10.3 at 25°C

27.09.2001 (42)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Oncorhynchus tschawytscha (Fish, fresh water, marine)
Exposure period	:	120 hour(s)
Unit	:	mg/l
LC100	:	= .9
LC10	:	= .5
Limit test	:	
Analytical monitoring	:	no
Method	:	other
Year	:	1952
GLP	:	no
Test substance	:	no data
Result	:	Other fish tested : - Silver salmon (Oncorhynchus kisutch) LC100 = 1.75 mg/l LC0 = 0.9 mg/l - Coastal cutthroat trout (Salmo clarki) LC100 = 1.2 mg/l LC0 = 0.7 mg/l
Source	:	Atofina, Paris-la-Défense, France.
Test condition	:	Test fishes King salmon (Oncorhynchus tschawytscha), Size 9-12 cm Silver salmon (Oncorhynchus kisutch), Size 7.5-11 cm Coastal cutthroat trout (Salmo clarki), Size 7.5-12 cm 10 fishes at each concentration Aquaria Cylindrical glass jugs of 18 l capacity and 86.6 sq. in. of air surface.No leakage. Temperature 17.5+-2°C for King salmon 15+-3°c for Silver salmon 12+-3°c for Coastal cutthroat trout Test solutions: - Dissolved oxygen 5 ppm - Free CO2 1.0-2.0 ppm - Methyl orange alkalinity (CaCO3) 20-65 ppm - Chlorine 0.1 ppm - Specific conductivity at 25 °C 1000-1200 *10-5 Mhos - pH 7.0-7.5
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

18.09.2001 (43)

Type	:	other
Species	:	Notropis atherinoides
Exposure period	:	120 hour(s)
Unit	:	mg/l
LC0	:	= .5
Limit test	:	
Analytical monitoring	:	no

Method	:	other
Year	:	1950
GLP	:	no
Test substance	:	no data
Remark	:	Also tested : Spot fin shiner (Notropis spilopterus)
Result	:	The result gives the concentration without mortality.
Source	:	Atofina, Paris-la-Défense, France.
Test condition	:	- A 0.1% stock solution of the tested substance was prepared - Water dilution standardized (no more details) - Temperature : adjusted from 11 to 20°C - Three to five fish were placed in the aquarium - The test was run for a maximum of 120 h.
Reliability	:	(3) invalid Documentation insufficient for assessment.

18.09.2001 (44)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static
Species	:	Daphnia sp. (Crustacea)
Exposure period	:	120 hour(s)
Unit	:	mg/l
LC0	:	= 1
Analytical monitoring	:	no
Method	:	other
Year	:	1950
GLP	:	no
Test substance	:	no data
Result	:	The result gives the concentration without mortality. Same test with : - May fly larvae (Blasturus and Leptophlebia) : LC0 = 1.0 mg/l - Cheronomus larvae : LC0 = 50.0 mg/l
Source	:	Atofina, Paris-la-Défense, France.
Test condition	:	- A 0.1% stock solution of the tested substance was prepared - Water dilution standardized (no more details) - Temperature : adjusted from 11 to 20°C - Daphnia were placed in the aquarium - The test was run for a maximum of 120 h.
Reliability	:	(3) invalid Documentation insufficient for assessment.

18.09.2001 (44)

Type	:	static
Species	:	Daphnia pulex (Crustacea)
Exposure period	:	
Unit	:	
Method	:	other: Werner's method
Year	:	1970
GLP	:	no
Test substance	:	no data
Result	:	It was impossible to determine the toxicity of methyl mercaptan.The analysis made indicated that it is transformed almost immediatly after introduction in the medium (rapid change from one level of oxidation to another) .
Source	:	Atofina, Paris-la-Défense, France.
Test condition	:	The test was made in glass cylinder of 110 ml capacity.The volume of the

test solution was 100 ml.The temperature was about 20°C.

18.09.2001 (45)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Ankistrodesmus falcatus (Algae)
Endpoint	:	biomass
Exposure period	:	
Unit	:	
Method	:	
Year	:	1976
GLP	:	
Test substance	:	other TS: 98% purity
Remark	:	It was shown that there was a highly significant positive correlation between chlorophyll a and cell counts (per volume) during the exponential growth period, about 3 days.After, the cell counts increased faster than chlorophyll a and after 4 days, the amount of hclorophyll a started deceasing.
Result	:	In this study, it was shown that methyl mercaptan at any concentration in 25% nutrient solution, i.e. 0.1, 1.0, 10.0, 50.0 and 100.0 mg/l, had no influence on the algal growth as determined by chlorophyll a measurements or cell counts, after 7 day exposition.
Source	:	Atofina, Paris-la-Défense, France.
Test condition	:	Culture conditions : Temperature : 20+-1°C Illumination : 3000 lux with daily rythm (14h light-10h dark) Algal were cultured in 100 ml nutrient solution in Erlenmeyer-lasks supported on a culture stand. Biomass titer tests were made in pyrex-test tubes closed with a paraffin film. The test substance was diluted to concentrations of 0.01, 0.1, 1.0 and 10.0 % and added to cultures which were in the exponential stage of growth with chlorophyll a values of 2.2 µg/ml. For the biomass titer test (BMT), effluent was diluted to concentrations of 0.1, 1.0 and 10.0 % with oligotrophic, humus-poor lake water, which was filtered and autoclaved for 20 min at 130°C. One drop of prediluted algal suspension was added to test tubes with 10 ml mixtures of lake water and test substance.No CO2 gas was fed into these cultures. Each test series had 3 replicates at each concentration. The growth was monitored daily for about one week by photometrically measuring the amount of chlorophyll a extracted with hot methanol. The number of cells per ml was counted under an inverted microscope. Both methods for determination of biomass, cell counts and measurement of chlorophyll content are internationally used in bio-tests.
Reliability	:	(4) not assignable Not appropiate.

28.09.2001 (46)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

Species	:	other terrestrial plant: Phaseolus vulgaris
Endpoint	:	
Exposure period	:	
Unit	:	
Remark	:	Seedlings of bush bean were exposed to methylmercaptan for 6 hours at a range of concentrations 6-82 µmol/m3 in an open gaseous exchange system, during which whole-plant net photosynthesis and transpiration were monitored. CH3SH caused no change in photosynthesis or foliar necrosis. Transpiration was affected: 78-86% of the control.
Source	:	Elf Aquitaine Lacq ECB - Existing Chemicals Ispra (VA)

23.10.1995 (47)

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Value	:	= 643 - 709 ppm
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	90
Vehicle	:	
Doses	:	
Exposure time	:	4 hour(s)
Method	:	other: equivalent to OECD Guide-line 403
Year	:	1981
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Method : Each dose group consisted of 5 male and 5 female rats, which were combined for a 4-h exposure or sham exposure to air in a customized 75-l glass chamber and then separated for observation over the subsequent 14-day period. Animals from any group that died during the 14-day period were examined for gross pathology, such as general or local haemorrhage and adhesions, and the survivors were sacrificed and examined as well. Mortality and such visually apparent behaviour as exploring, huddling, preening, and obvious distress were noted during the courses of the 4-hour exposures and sham exposures. The rats were deprived of food and water during actual exposure or sham exposure. LC50 values and 95% confidence limits were estimated by the classical method of Litchfield and Wilcoxon (1949).

Result : The table summarizes the 14-d, 4-h LC50 determinations for methyl mercaptan. In all cases, any animal that survived the first 24 h after exposure survived to the end of the 2-wk observational period. There was no evidence of external bleeding from any orifice in rats that succumbed or survived.

Dose-Response Summary for Acute Inhalatory Exposures

Dose (ppm)	Mortality (male and female combined)
Sham	0/10
400	0/10
600	2/10
650	5/10
680	4/10
690	4/10
700	10/10
700	10/10
800	10/10

- LC50 = 675 (643-709) ppm

Source : Atofina, Paris-la-Défense, France.

Reliability : (2) valid with restrictions
Flag : Directive 67/548/EEC, Critical study for SIDS endpoint
11.01.2001 (48)

Type : LC50
Value : = 1428 - 1980 ppm
Species : rat
Strain : other: WBS/W
Sex : male
Number of animals : 24
Vehicle :
Doses :
Exposure time : 1 hour(s)
Method : other
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Two rats (c.a. 200 g) were placed in each of a series of 20-liter exposure chambers and the latter sealed air-tight. a small volume of air was withdrawn from each chamber and replaced with the required volume of sample. Inhalation exposure was terminated sixty minutes later and the surviving animals were observed for seven days. The sample was measured and dispensed under ambient conditions of temperature and pressure by means of dry glass syringes. The volumes of the gas used to produce the concentrations 20, 28, 40, and 56 ml respectively.

Result : - Mortality:

Vapor conc. ppm	# rats dead/total	Mortality	time for death minutes					
1000	0/6	0%	-	-	-	-	-	-
1400	1/6	17%	-	-	-	-	-	51
2000	5/6	83%	-	22	22	27	33	43
2800	6/6	100%	l0	11	11	12	13	13

- LC50 = 1680 ppm (1428-1980 = 95% confidence limits).

- Symptomatology: dyspnea, ataxia, loss of righting reflex (anesthesia), progressive respiratory depression, and cyanosis. Surviving animals showed signs of dyspnea only.

Source : Atofina, Paris-la-Défense, France.
Reliability : (3) invalid
10.08.2001 (49)

Type : LCLo
Value :
Species : rat
Strain : no data
Sex : female
Number of animals : 4
Vehicle :
Doses :
Exposure time :
Method : other
Year :
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : In each experiment one rat was placed in a gas chamber of 7 liters volume and exposed for a maximum of 30-35 min to controled concentrations of

methyl mercaptan.

Result :

Concentration mg/l	ppm	Effect
1	500	No effect in 30 minutes.
1.4	700	The rat seemed tired, but recovered instantly when taken out.
3	1500	After 15 min, the rat could keep on its legs but obviously only with great difficulty. At the end of the experiment it could get up for a moment but then trembled all over its body. Recovery in 5 minutes. Microscopically, clustered changes of edema type: thickened alveolar walls, exudation in the alveoli containing blood cells.
20	10000	Convulsions after 1 min. After 2 min fast and superficial respiration. After 6 min, the rat lay on side. After 8 min, respiration irregular. After 14 min, the respiration stopped. Autopsy: macroscopically, small bleedings in the lungs. Microscopically: alveoli stuffed with erythrocytes, large aresa, compensatory emphysema. Moderate amounts of serous fluid in the alveoli.

: Atofina, Paris-la-Défense, France.

Reliability : (3) invalid
20.08.2001 (50)

5.1.3 ACUTE DERMAL TOXICITY

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

5.2.2 EYE IRRITATION

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Type :
Species : rat
Sex : male
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : 3 months
Frequency of treatm. : 7 h/day ; 5 d/week
Post exposure period : none
Doses : 2, 17, 57 ppm

Control group : yes, concurrent no treatment
NOAEL : = 17 ppm
LOAEL : = 57 ppm
Method : other: not specified
Year : 1981
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : Groups of male Sprague-Dawley rats (31/group) were exposed whole-body to concentrations of 0, 2, 17 or 57 ppm methyl mercaptan for 7 hrs/day, 5 days/week for an overall period of 3 months.
All animals were kept in closed colony cages (6 per cage) under controlled conditions of temperature and illumination for 1 wk before being committed to an experiment in order to screen for sicke, suspicious, or overly aggressive types. A subset of 10 animals from each group was designated for special metabolic performance studies by an independent true random process. To minimize possible differences in feeding behavior during exposure periods, the sham and experimental groups were deprived of food during the exposure periods. Tap water was provided ad libitum. At the end of the exposure day the metabolic subsets were placed overnight in metabolism cages and the appropriate measurements were made. Metabolic performance measurements were made for 17 h periods on 5 consecutive days.
At the end of the 3-mo experimental period the metabolic subsets served as the subjects for the following tests: intestinal transit time, systolic blood pressure effects, and histological examination of selected organs (heart, lungs, small intestine, liver, and kidneys). The observations were made at least 24 h later than the end of the last exposure day. Other biological data, obtained from the balance of the animals, included terminal body weight, O2 consumption, SMA 12/60 blood analyses, and organ weights (brain, lung, liver, spleen, heart, kidneys, and adrenals).
Complete histopathologies of livers of the 84 remaining sham and exposed rats were performed.

Result : No mortality response was observed in any sham or exposed population of rats during the 3-mo period. However, during actual exposures the rats tended to huddle in groups of 5 or 6 toward the periphery of the chamber with noses pointed outward from the chamber's vertical axis. This behavior was not observed in the sham group but was markedly obvious at 57 ppm. Average terminal body weights were lower than those of sham controls for all rats in the exposed groups. This difference was statistically significant in the 57 ppm group and showed a statistically significant dose-related trend (Table 1). The same was true when average rates of body weight increases were determined by regression analyses for the metabolic subsets.

Table 1. Changes in Body and Normalized Tissue Wet Weights (g) Resulting from 3-mo Exposure to Methyl Mercaptan Vapor

	Experimental group			
Tissue	0 ppm	2 ppm	17 ppm	57 ppm
-Whole body	458.6±53.5	446.5±48.6	443.4±45.6	391.7±45.0*#
Brain	0.44±0.06	0.45±0.05	0.44±0.09	0.49±0.09*
Lung	0.35±0.07	0.32±0.05	0.35±0.07	0.34±0.05
Liver	2.78±0.41	2.81±0.46	2.84±0.46	2.75±0.43
Spleen	0.16±0.02	0.15±0.03	0.15±0.02*	0.18±0.02*
Heart	0.29±0.03	0.30±0.03	0.29±0.04	0.28±0.03
Kidneys	0.66±0.05	0.64±0.06	0.65±0.05	0.64±0.05
Adrenals	0.012±0.004	0.011±0.002	0.010±0.002*	0.017±0.007*

-Mean±SD represents 31 animals in each group.
* Statistically significant difference compared with the mean values for sham control rats ($p<0.015$ for each pairing; $p<0.05$ overall).
# Dose-related change statistically significant at 95% confidence level.

Although some average organ weights were significantly different from corresponding sham values (Table 1), there was no obvious dose-related trend such as was apparent with whole-body weights, these significant differences could be due to chance alone.

Average rates of change of food intake and wet and dry fecal weights were not significantly different from those of the sham controls. Fecal pellet production rate increases (data not shown) were significantly lower for the 2 and 17 ppm subsets and nonsignificantly greater for the 57 ppm subset. Rates of water intake increase were less for all exposed subsets, although this was not significant for the 57 ppm subset. Rates of water output increase were slightly higher for all exposed subsets, although the rate of increase for the 57 ppm subset was not significant.

Statistically significant changes were observed in serum components of terminal blood samples from animals of all exposed groups subjected to SMA 12/60 analysis (Table 2). Average total serum proteins were significantly higher for all exposed groups. Average albumin concentrations were significantly lower for all exposed groups. Significant reductions in inorganic phosphate occurred in the 2 and 17 ppm groups. Cholesterol was significantly elevated in the 2 ppm group and total bilirubin was significantly higher in the 2 and 17 ppm groups. Blood urea N vas significantly lower in the 57 ppm group and lactate dehydrogenase was significantly lower in all three exposed groups. None of these trends were dose-related at the 95% confidence level.

Table 2. SMA 12/60 Blood Serum Analyses after 3-mo Exposure to Methyl Mercaptan Vapor

	Experimental group			
Tissue	0 ppm	2 ppm	17 ppm	57 ppm
-Total protein (g%)	6.69±0.49	7.23±0.53*	7.47±0.54*	7.14±0.85*
Albumin (g%)	3.44±0.25	3.00±0.22*	2.99±0.20*	2.92±0.25*
Ca2+ (mg%)	4.92±0.32	5.01±0.28	5.03±0.30	4.90±0.55
Pi (mg%P)	8.25±1.10	7.40±0.79*	7.49±0.63*	7.73±0.58
Cholesterol (mg%)	65.8±15.2	75.7±13.8*	69.1±9.3	66.4±16.4
BUN (mg%)	22.48±3.61	23.68±5.37	22.27±3.63	20.00±3.54*
Uric acid (mg%)	1.86±0.75	1.68±0.41	1.70±0.41	1.44±0.59
Total bilirubin (mg%)	0.11±0.08	0.41±0.26*	0.43±0.19*	0.09±0.14
Alkaline phosphatase (mU/ml)	241.6±99.0	209.3±92.2	210.1±81.3	248.9±112.9
LDH (mU/ml)	597±130	465±146*	468±116*	522±100*
SGPT (mU/ml)	86±28	77±20	77±19	87±27
SGOT (mU/ml)	301±74	276±46	273±49	277±55
Glucose (mg%)	122.8±18.3	125.2±16.7	123.5±18.0	133.0±20.8

-A total of 31 rats were used at each dose level. Values are expressed as mean ± SD.
Abbreviations: SMA, sequential multiple analyzer; Pi, inorganic phosphate; BUN, blood urea N; LDH, lactic dehydrogenase; SGPT, serum glutamic-pyruvic transaminase; and SGOT, serum glutamic-oxaloacetic transaminase.
* Statistically significant difference compared with mean values for sham

control rats ($p<0.015$ for each pairing; $p<0.05$ overall).

No significant differences in intestinal transit performance parameters were observed in any of the metabolic performance subsets.
No consistent patterns were observed in average values of systolic blood pressure in the metabolic subset rats. After week 1, average values of O2 consumption measured in special subsets tended to be lower for exposed than for sham rats, but the differences were not consistently significant. All of these average values tended to decrease with time during the limited course of the observations. However, for both the sham and exposed groups the mean 02 consumption rates are higher than those expected for normal rats. These studies could not be conducted beyond 3 week because the rats grew too large to fit into the apparatus used for measuring O2 consumption.

Routine histopathological examination was conducted for five rats per dose group and was negative for the heart, small bowel, and kidneys. Lungs exhibited the pneumonia, emphysematic changes, and occasional fibrosis that are characteristic of rat colonies. These pictures did not appear to be different in samples from exposed rats. Some evidence of pathological changes was noted in liver sections from 31 rats each in the 2, 17, and 57 ppm groups. In all cases there was evidence of inflammatory cells and possibly enlarged bile ductules. Hyperplastic nodules were observed in one liver section from the 2 ppm and in three liver sections from the 57 ppm group. One hepatic carcinoma was visually observed (and sampled for histopathological examination) on the ventral surface of the liver of a rat in the 17 ppm group. In the case of the sham control group, 31 livers were hand-sectioned (2-3 µm) and examined under a dissecting microscope. Two small nodular lesions were detected in two livers; under light microscopy they were observed to be a hyperplastic region similar to that observed in the 2 and 57 ppm groups. Therefore, the treatment relationship of the hyperplastic nodules observed in the treated animals can be ruled out.

Source : Atofina, Paris-la-Défense, France.
Reliability : (2) valid with restriction
20.08.2001 (48)

5.5 GENETIC TOXICITY 'IN VITRO'

5.6 GENETIC TOXICITY 'IN VIVO'

Type : Micronucleus assay
Species : mouse
Sex : male/female
Strain : Swiss Webster
Route of admin. : inhalation
Exposure period : 6 hours
Doses : 0, 114, 258 and 512 ppm
Result : negative
Method : OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year : 1983
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : The genotoxic potential of nose-only inhalation exposure of methyl mercaptan to induce micronucleus formation in bone marrow erythrocytes was determined in Swiss-Webster mice.

In the dose-range finding study, three mice per sex per treatment group received a single 6-hour nose-only inhalation exposure to methyl mercaptan at 112, 374, and 570 ppm. A control group, consisting of three male and three female mice, received air only. Mice were observed daily from the start of treatment until death or sacrifice. The concentration ranges for the low- and mid-concentrations exceeded the protocol criterion of 10%. These deviations are judged not to have had a significant adverse effect on the study.

In the definitive experiment, 15 mice per sex per treatment group were exposed to methyl mercaptan by nose-only inhalation at 114, 258, or 512 ppm. Five mice per sex per group were sacrificed 24, 48, and 72 hours cytotoxicity and micronucleus formation. An air-exposed control group of male and female mice and a urethane positive control group of male mice were treated similarly and evaluated concurrently with the methyl mercaptan-treated groups.

Result : DOSE RANGE FINDING EXPERIMENT
No significant differences as observed between terminal and pre-exposure body weights of each of the treatment groups at each of the sacrifice times. Clinical signs observed included shallow breathing at the fourth hour of exposure at 112 ppm, shallow breathing at the third hour of exposure at 374 and 570 ppm with hypoactivity at the mid and high dose levels in all mice when observed after completion of exposure. Two male mice were found dead near the end of the second hour and during the sixth hour of exposure at 570 ppm. Any mouse showing clinical signs appeared normal on Day 2. Surviving mice were sacrificed approximately 72 hours after the inhalation exposure, and cytotoxicity was determined based on the ratio of RNA-positive erythrocytes (PCEs) to total red blood cells (RBCs) in both peripheral blood and bone marrow smears. No significant PCE suppression was observed in any of the methyl mercaptan treatment groups when compared to the air control group in either peripheral blood or bone marrow.

DEFINITIVE EXPERIMENT
Clinical observations in this experiment included shallow breathing and hypoactivity at the fourth and fifth hours, respectively, of exposure at 258 ppm in all mice. All mice at 258 ppm appeared normal on Day 2 and on all subsequent experiment days. Shallow breathing at the third and fourth hours of exposure, and hypoactivity at the fifth hour of exposure were observed at 512 ppm in all mice. One female mouse was found dead after 2 hours of exposure at 512 ppm, and two female and two male mice were found dead at 512 ppm on Day 2. All surviving mice at 512 ppm appeared normal on Day 2 and on all subsequent experiment days. Mice treated with 114 ppm methyl mercaptan, air control, or urethane appeared normal throughout the experiment. The percentages of PCEs among RBCs in groups treated with methyl mercaptan did not differ significantly from those of the air control groups in any of the dose groups for either sex.
In male mice, none of the individual dose groups had a statistically significant increase in MN frequency. Using the Cochran-Armitage test for a trend in binomial proportions, a statistically significant upward trend in micronucleus (MN) frequency was observed in female mice sacrificed at 24 hr after exposure to the methyl mercaptan.
However, the MN frequency in the control group was lower than the laboratory historical value (0.21%) for females of this strain of mice, and none of the individual dose groups had a statistically significant increase in MN frequency.

DEFINITIVE EXPERIMENT IN MALE SWISS-WEBSTER MICE TREATED WITH A SINGLE EXPOSURE OF METHYL MERCAPTAN: MICRONUCLEUS FREQUENCY

Dose	Time	PCE/RBC (%)	PCE with MN

(ppm)	(hrs)	nb	Mean±S.E.	Mean±S.E.
0.0	24	5	57.10±4.18	0.13±0.02
114.0	24	5	57.61±5.09	0.15±0.03
258.0	24	5	52.27±7.70	0.16±0.02
512.0	24	5	45.46±5.45	0.18±0.02
Urethane	24	5	52.84±5.69	0.65±O.l0*
0.0	48	5	51.31±4.83	0.18±0.05
114.0	48	5	52.93±6.80	0.13±0.03
258.0	48	5	47.05±3.88	0.17±0.02
512.0	48	5	49.25±2.22	0.17±0.03
Urethane	48	5	40.09±3.66	0.45±O.ll*
0.0	72	5	52.76±4.12	0.10±0.03
114.0	72	5	44.16±5.90	0.15±0.04
258.0	72	5	42.56±6.87	0.09±0.01
512.0	72	3	52.35±2.47	0.18±0.03
Urethane	72	5	42.54±3.08	0.22±0.02*

* Statistically different from control ($p < 0.01$) by test for binomial proportions.

DEFINITIVE EXPERIMENT IN FEMALE SWISS-WEBSTER MICE TREATED WITH A SINGLE EXPOSURE OF METHYL MERCAPTAN: MICRONUCLEUS FREQUENCY

Dose (ppm)	Time (hrs)	nb	PCE/RBC (%) Mean±S.E.	PCE with MN Mean±S.E.
0.0	24	5	47.39±4.67	0.09±0.02
114.0	24	5	52.83±4.60	0.10±0.03
258.0	24	5	53.68±3.04	0.12±0.03
512.0	24	4	49.98±2.07	0.17±0.04
0.0	48	5	49.06±2.24	0.12±0.05
114.0	48	5	56.58±2.60	0.13±0.04
258.0	48	5	58.73±3.76	0.13±0.02
512.0	48	5	50.07±3.96	0.17±0.05
0.0	72	5	59.41±7.54	0.10±0.04
114.0	72	5	55.66±4.10	0.13±0.04
258.0	72	5	52.46±3.85	0.12±0.03
512.0	72	3	51.96±4.98	0.16±0.04

Source : Atofina, Paris-la-Défense, France.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
10.08.2001

(51)

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

Remark : A 53 year old black worker was hospitalized because of coma appearing shortly after heavy exposure to methanethiol. Acute, severe hemolytic anemia and methemoglobinemia developed : both were brief in duration. The likely mechanism of the hemolysis was an oxidant effect of methanethiol in a person deficient in erythrocytic glucose-6-phosphate dehydrogenase (G-6-PD). Deep coma persisted until death 28 days after exposure to the chemical agent.

Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

23.10.1995 (52)

Remark : This study investigated a possible relationship between exposure to sufides and disturbances of the synthesis of heme and the erythrocytes. Eighteen workers exposed to sulfides at a pulp and paper plant were examined and compared with individually matched referents from a thermomechanical pulp plant without such exposure. The exposure levels of methylmercaptan were low. However, five subjects were exposed to high levels of short duration, and their data were analyzed separately. The activity of the enzymes delta-aminolevulinic acid synthase and heme-synthase in reticulocytes, characteritics of the erythrocytes, and the iron status were analyzed. A minor decrease, not statistically significant, was observed for the enzymes among the five highly exposed subjects. However, the concentrations of iron and transferrin were elevated and the concentration of ferritin was low in comparison to the corresponding levels of the referents. This combination will not occur spontaneously. A previous study indicated that sulfides may inhibit heme synthesis, and the present study suggests that they may also disturb iron metabolism.

Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

10.08.2001 (53)

Remark : The ASTDR statement about the possible inherited erythrocytic glucose-6-phosphate dehydrogenase deficiency follows : Although hemolysis may occur in any person who is exposed to a sufficiently high dose of methyl mercaptan, this enzyme defficiency may cause some persons to be unsually sensitive, since it results in an inability to maintain reduced glutathione which is needed for the integrity of the erythrocyte membrane. The incidence of the deficiency among Caucasians of European origin is relatively low, whereas there is a higher incidence among certain groups of Asians and Mediterranean (Italians, Sardinians, Greeks), and Middle Eastern populations. A study of hemolytic anemia in American Black children with G-6-PD deficiency suggests that this is another population that may be susceptible to the hemolytic effects of methyl mercaptan exposure. A syndrome of acute severe hemolysis following exposure to oxidative stress is associated with the Mediterranean variant of the deficiency, whereas the hemolytic anemia seen in American Blacks is generally (this deficiency is estimated to 16% Black males or 10% sex not specified). The pattern of inheritance for G-6-PD deficiency is that of an

autonomous sex-linked defect. This is an X-linked disorder and is thus fully expressed in males who carry it on their single X chromosome and in females who carry it on both X chromosomes. Female heterozygotes (who have one normal and one defective gene for this trait) have a wide variery of values for the enzyme which suggests that other factors influence the degree to which this trait is influenced in identical genotypes.

Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

13.02.2001 (54)

5.11 ADDITIONAL REMARKS

Type : Biochemical or cellular interactions

Remark : If methane thiol introduction into the system exceeds the saturation and normal metabolizable capacity, it becomes bound to protein and erythrocytes. Thus it indirectly decreases the vascular oxygen carrying capacity. Methylmercaptan also inhibits several enzyme systems such as carbonic anhydrase, beta-tyrosinase and Na+, K+ -ATPase. The enzyme inhibition appears to be related to a thiol-metal interference. Thus in turn affects the bioelectric activity of various systems, such as the respiratory muscles of mammals. Several authors.

Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

Reliability : (4) not assignable
13.02.2001 (55)

Type : Biochemical or cellular interactions

Remark : Methanethiol inhibited glutaminase activity of the synaptosomal mitochondria from the cerebrum and brain stem of rats. These neurotoxic substances might cause hepatic encephalopathy by decreasing the synthesis and release of the excitatory neurotransmitters such as glutamic acid.

Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

Reliability : (2) valid with restrictions
13.02.2001 (56)

Type : Biochemical or cellular interactions

Remark : In rats with acute hepatic encephalopathy caused by liver ischemia and in dogs suffering from hepatic encephalopathy resulting from chronic liver disease, large and significant increases in ammonia levels were measured. However, the mean levels of methanethiol mixed disulfides in rats and dogs with hepatic encephalopathy were not different from the mean normal levels in these animals. It is concluded that in these animal models of liver failure the role of methanethiol in the pathogenesis of hepatic encephalopathy
is probably minor or insignificant.

Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

Reliability : (2) valid with restrictions
13.02.2001 (57)

Type : Biochemical or cellular interactions

Remark : The synthesis in human organism is confirmed by its occurence in mouth and crevicular air of individuals with active periodontal disease (anaerobic fermentation). Even low concentration of CH3SH has a significant adverse

effect on proline transport.

Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)

23.10.1995 (58)

Type : Metabolism

Remark : Methyl mercaptan appears in urine within an hour after eating asparagus.
Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)
Reliability : (4) not assignable
13.02.2001 (59)

Type : Metabolism

Remark : Methyl mercaptan was metabolized to carbon dioxide and sulfate by rats. The sulfate was excreted in the urine and 94 % of the sulfur of methanethiol was removed from the body within 21 hr. Ammonia had no effect on methanethiol metabolism. Rats in a coma from octanoate or due to heptic necrosis excreted little sulfate in the urine.
Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)
Reliability : (4) not assignable
13.02.2001 (59)

Type : other

Remark : Methyl mercaptan is a food additive permitted for direct addition to food for human consumption, as long as 1) the quantity added to food does not exceed the amount reasonably required to accomplish its intended physical, nutritive, or other technical effect in food, and 2) when intended for use in or on food it is of appropriate food grade and is prepared and handled as a food ingredient.
Source : Elf Aquitaine Lacq
ECB - Existing Chemicals Ispra (VA)
Reliability : (4) not assignable
20.08.2001 (59)

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I U C L I D

Data Set

Existing Chemical	:	ID: 5188-07-8
CAS No.	:	5188-07-8
EINECS Name	:	sodium methanethiolate
EC No.	:	225-969-9
Molecular Formula	:	CH4S.Na

Producer related part

Company	:	Atofina
Creation date	:	10.01.2001

Substance related part

Company	:	Atofina
Creation date	:	10.01.2001
Status	:	
Memo	:	
Printing date	:	26.10.2001
Revision date	:	
Date of last update	:	28.09.2001
Number of pages	:	21
Chapter (profile)	:	Chapter: 2, 3, 4, 5
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

2.1 MELTING POINT

Decomposition	:	, at > 210 °C
Sublimation	:	
Method	:	
Year	:	2000
GLP	:	
Test substance	:	
Remark	:	Cristallisation temperature: ca. 55°C
Source	:	Atofina, Paris la Défense
Reliability	:	(2) valid with restrictions Data from Laboratory testing Atofina Netherlands

01.08.2001

2.2 BOILING POINT

Value	:	= 69 °C at
Source	:	Atofina, Paris la Défense
Reliability	:	(2) valid with restrictions

01.08.2001 (1)

2.3 DENSITY

Type	:	relative density
Value	:	= 1.324 at 20 °C
Source	:	Atofina, Paris la Défense
Reliability	:	(2) valid with restrictions Data from Laboratory testing Atofina Netherlands

01.08.2001

Type	:	relative density
Value	:	= 1.25 at 70 °C
Source	:	Atofina, Paris-la-Défense, France.
Reliability	:	(2) valid with restrictions Data from Laboratory testing Atofina Netherlands

01.08.2001

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

2.5 PARTITION COEFFICIENT

Partition coefficient	:	
Log pow	:	= -2.33 at °C
pH value	:	
Method	:	other (calculated)

Year	:	
GLP	:	
Test substance	:	

28.09.2001 (2)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value	:	> 23 °C
Type	:	
Method	:	Directive 84/449/EEC, A.9 "Flash point"
Year	:	
GLP	:	
Test substance	:	
Source	:	Atofina, Paris la Défense
Reliability	:	(2) valid with restrictions

01.08.2001 (1)

2.8 AUTO FLAMMABILITY

Value	:	> 350 °C at
Source	:	Atofina, Paris la Défense

01.08.2001 (1)

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

3.1.2 STABILITY IN WATER

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum :
Concentration : 10 mg/l related to COD (Chemical Oxygen Demand)
20 mg/l related to COD (Chemical Oxygen Demand)
Contact time : 28 day(s)
Degradation : = 64 (±) % after 21 day(s)
Result : readily biodegradable
Kinetic of testsubst. : 7 day(s) = 7 %
14 day(s) = 55 %
21 day(s) = 64 %
28 day(s) = 58 %
%
Control substance : Benzoic acid, sodium salt
Kinetic : 7 day(s) = 78 %
14 day(s) = 88 %
Deg. product : not measured
Method : OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year : 1995
GLP : no
Test substance : **Sodium methyl mercaptide**, purity : not reported.
Results

Dissolved Oxygen					
	Day				
	0	**7**	**14**	**21**	**28**
1-Medium+inoculum	8.76 8.76 Mean : 8.76	8.26 8.46 Mean : 8.36	8.56 8.24 Mean : 8.40	8.36 8.12 Mean : 8.24	7.62 7.86 Mean : 7.74

2-Medium+Inoculum+test Substance	8.12 8.16 8.12 Mean : 8.13	7.33 7.33 7.21 mean : 7.29	4.02 4.02 4.10 Mean : 4.05	3.31 3.27 3.27 Mean : 3.28	3.23 3.27 3.15 Mean : 3.22
3-Medium+Inoculum+Test Substance+ reference	8.16 8.12 Mean : 8.14	3.89 4.01 Mea : 3.95	2.92 3.04 Mean : 2.98	3.03 3.19 Mean : 3.11	3.15 2.99 Mean : 3.07
4-Medium+Inoculum+ reference	8.76 8.76 Mean :8.76	3.16 3.12 Mean : 3.14	2.31 2.68 Mean : 2.50	2.67 2.79 Mean : 2.73	2.39 2.19 Mean : 2.29

	COD or ThOD (mgO2/mg)	Concentration (mg/l) serie 2 Serie 3 Serie 4
Test substance	0.34	20 10
Sodium benzoate	1.67	2 4
Serie **3**	0.56	

BOD (O2 mg/mg substance)					
Day	0	7	14	21	28
Serie 2 (substance)	0	0.02	0.19	0.22	0.19
Serie 3 (inhibition control)	0	0.32	0.40	0.38	0.34
Serie 4 (reference)	0	1.31	1.48	1.38	1.36
Biodegradation %					
Day	0	7	14	21	28
Serie 2 (substance)	0	7	55	64	58
Serie 3 (inhibition control)	0	57	72	67	60
Serie 4 (reference)	0	78	88	82	82

Rev. note The % degradation of the reference substance has reached the level for ready biodegradability by 14 days.
The difference of extremes of replicate values of the removal of test chemical (serie 2) is less then 20%.The degradation of the reference chemical in serie 3 is > 25% in the first 14 days.The test chemical is not inhibitory.
Oxygen depletion in the inoculum blank did not exceed 1.5 mg/l dissolved O2 after 28 days.
The residual concentration of oxygen in the test bottles did not fall below 0.5 mg/l at any time.

Source : Atofina, Paris-la-Défense, France.
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
28.09.2001 (3)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	= 1.32 - 2.46
EC50 24hrs	:	= 4.38 - 7.37
Analytical monitoring	:	yes
Method	:	OECD Guide-line 202
Year	:	2000
GLP	:	yes
Test substance	:	other TS: 32.9% purity in water

Method : Daphnids were exposed in a static test to a concentration range of 0.83 to 7.47 mg/l, forming a geometric progression with a factor of 1.7. The test was performed with 20 daphnids per concentration. Testing flasks were incubated in darkness at 19±1°C.

For each exposure concentration, the percentage of immobilisation after 24 hours and 48 hours was recorded. EC50-24h and EC50-48h were evaluated in the measured concentration range of 1.32-2.46 mg/l for EC50-48h and 4.38-17.37 mg/1 for EC50-24h.

The appearance of the test solution was visually checked at the beginning. and at the end of the test. Solutions were found to be clear, colourless over the period of the test. No precipitation was observed at the end of the test.

The study was performed in compliance with its quality criteria : immobilisation in the control did not exceed 10% at the end of the test ; test daphnids in the control were not trapped at the surface of the water; concentration of dissolved oxygen in the test vessel remained above 2 mg/l at end of the test and pH did not vary by more than 1 unit; the concentrations of the test substance have been maintained to within 80 % of the initial concentration throughout the duration of the test.

Result : - Biological observations

C nom mg/l	% imm	1	2	3	4	total
5.00	100	0	0	0	0	0
2.90	100	0	0	0	0	0
1.70	100	0	0	0	0	0
1.00	10	4	5	4	5	18
0.60	0	5	5	5	5	20
0	0	5	5	5	5	20

Control response was satisfactory.

- Concentrations

Measured		
Initial	Final	Final/Initial

mg/l	mg/l	%
0.83	0.81	98
1,32	1.23	93
2.46	2.47	100
4.38	4.25	100
7.47	6.45	86

DL (Detection Limit) : 0.1741 mg/l

Source : ATOFINA Chemicals Inc. Philadelphia

Test condition : - Test organisms :
Daphnia magna Straus Clone A from INERIS, France.
Breeding colony realized in the laboratory in an Elendt M7 medium , supplemented with algal based feed. Organisms are selected by sieving.
Age at study initiation < 24h old.

- A stock solution is prepared before the beginning of the test, by vigorously mixing during 24 hours 8 mg of the substance with 1 liter of dilution water.

- Test temperature range : 20-21°C

- Exposure vessel :
Closed flasks as test glassware entirely filled with test solutions and stoppered with PTFE bungs and sealed with aluminum caps

- Dilution water :
Prepared in the laboratory using pure water and salts according to ISO 6341.
25 ml/l of the below solutions , aerated up to oxygen saturated
11.76 g CaCl2, 2 H2O /l ultrapure water
4.93 g MgSO4, 7 H2O /l ultrapure water
2.59 g NaHCO3 /l ultrapure water
0.23 g KCl /l ultrapure water

- Dilution water chemistry :
According to ISO 6341
Ca+Mg ions = 2.5 mmol/l.
Ca/Mg = 4
Na/K = 10
pH 7.8 ± 0.2

- Water chemistry in test :

C (nom)	pH		dissolved O2 (mg/l)	
mg/l	T0	T48h	T0	T48h
0	7.96	7.95	9.4	9.0
0.6	7.96	7.93	9.6	9.2
1.0	7.96	7.94	9.5	9.3
1.7	7.97	8.03	9.5	9.3
2.9	8.10	8.09	9.5	9.2
5.0	8.19	8.22	9.6	9.2

- Test design
4 replicates , 5 individuals per replicate

- Analytical monitoring : liquid chromatography/mass spectrometry

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

28.09.2001 (4)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	= 75 - 161 mg/kg bw
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	40
Vehicle	:	water
Doses	:	
Method	:	OECD Guide-line 401 "Acute Oral Toxicity"
Year	:	1981
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : In a first assay, Sodium methylmercaptide (19.9% solution in water), was administered in its original form to a group of 10 Sprague-Dawley rats (5 males and 5 females) at a dose level of 2000 mg/kg at a volume of 2.05 ml/kg taking into consideration that the specific gravity (SG) of the test substance was 0.977. In a second assay, the test substance was administered at the dose levels of 400, 620, 950 and 1400 mg/kg to 4 groups of 5 males and at the dose levels of 620 and 950 mg/kg to 2 groups of 5 females. The test substance in aqueous solution was administered at a volume of 10 ml/kg. All animals were fasted before treatment.

Dose (mg/kg)				
19.9% solution	Active material	Volume (ml/kg)	number of animals	
			male	female
400	80	10	5	
620	123	10	5	5
950	189	10	5	5
1400	279	10	5	
2000 (undilut.)	398	2.05	5	5

The mortality, general behaviour and bodyweight gain of the animals were observed for a period of 14 days after the single administration of the test substance. A necropsy was performed on each animal found dead or sacrificed at the end of the study. The LD50 in males was calculated according to Finney's method.

Result : The mortality was respectively 20%, 40%, 100%, 100% and 100% at the dose levels of 400, 620, 950, 1400 and 2000 mg/kg in the males and 60%, 100% and 80 % at the dose levels of 620, 950 and 2000 mg/kg in the females. Mortality was recorded within minutes of treatment.

A significant decrease in spontaneous activity, dyspnea at the dose levels of 400 and 620 mg/kg, tonico-clonic convulsions at the dose levels of 950 and 1400 mg/kg before death of the rats, and ataxia and coma at the dose level of 2000 mg/kg were the main clinical signs recorded.

The bodyweight gain of the surviving animals was normal at the dose level of 400 mg/kg and slackened off slightly until D5 at 620 and 2000 mg/kg.

An abnormal red colouration of the stomach was observed during the macroscopic examination of all animals from all dose levels found dead during the study.

The necropsy performed on animals sacrificed at the end of the study revealed no macroscopic abnomalities.

Source : Atofina, Paris-la-Défense, France.

Test substance : The test article used as such was :
CH3SNa : 19.9% solution in water
Na2S : 0.30%
Free NaOH : 1.1%
Releasable NaOH: 12.75%

Conclusion : The LD50 of the test substance METHYL MERCAPTIDE DE SODIUM, SOLUTION AQUEUSE A 18 % administered by oral route in the male Rat was 581 (376-810) mg/kg using the formulated test substance or 116 (75-161) mg/kg using the pure test substance. The test substance toxicity in the females was similar to that of the males.

Reliability : (1) valid without restriction

Flag : Directive 67/548/EEC, Critical study for SIDS endpoint

13.08.2001 (5)

Type : LD50

Value : = 84 - 146 mg/kg bw

Species : rat

Strain : Sprague-Dawley

Sex : male/female

Number of animals : 40

Vehicle : water

Doses :

Method : OECD Guide-line 401 "Acute Oral Toxicity"

Year : 1981

GLP : yes

Test substance : as prescribed by 1.1 - 1.4

Method : Sodium methylmercaptide (19.6% solution in methanol), undiluted or diluted with water, was administered by gavage to male and female rats according to the following table:

Dose (mg/kg)				
19.6% solution	Active material	Volume (ml/kg)	number of animals	
			male	female
300	59	10	5	
420	82	10	5	5
580	114	10	5	5
820	161	10	5	
2000 (undilut.)	392	2.18	5	5

The mortality, general behaviour and bodyweight gain of the animals were observed for a period of 14 days after the single administration. A necropsy was performed on each animal found dead during the study or sacrificed at the end of the study. The LD50 was calculated according to Finney's method.

Result : - Mortality:

Dose (mg/kg)			
19.6% solution	Active material	% of mortality	
		male	female
300	59	0	
420	82	20	0
580	114	40	40
820	161	100	
2000 (undilut.)	392	100	100

- LD50: 109 (84-146) mg/kg (active material)

- Clinical signs :
. decrease spontaneous activity at 300 and 420 mg/kg,
. marked decrease in spontaneous activity and tonic-clonic convulsions at 580 and 820 mg/kg,
. ataxia accompagnied by sedation and lateral recumbency followed by coma at 2000 mg/kg.

- Occurence of death : 5 to 30 minutes after gavage.

- The macroscopic examination of animals found dead during the study revealed an abnormal appearance of the stomach in 2 rats at 800 mg/kg and in all rats at 2000 mg/kg.
The necropsy of the animals found dead during the study or sacrified at the end of the study revealed no macroscopic abnormalities at 300, 420 and 580 mg/kg.

Source : Atofina, Paris-la-Défense, France.
Test substance : The test article used as such was :
CH3SNa : 19.6% solution in methanol
Na2S : 1%
Free NaOH : =< 0.1%
Releasable NaOH: 12.2%
Reliability : (1) valid without restriction
Flag : Directive 67/548/EEC, Critical study for SIDS endpoint
13.08.2001 (6)

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

Type : LD0
Value : > 84.8 mg/kg bw
Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 20
Vehicle : water
Doses :
Method : OECD Guide-line 402 "Acute dermal Toxicity"
Year : 1987
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Sodium methylmercaptide (21.2% solution in water) was administered by dermal route to a group of 10 Sprague-Dawley rats (5 males and 5

females).

As the test substance was anticipated to be corrosive, 2 animals were used in a first assay. The test substance in its original form was applied directly to the skin at a dose of 2000 mg/kg (i.e. 424 mg/kg in raw material), taking into consideration that the specific gravity (SG) of the test substance was 1.12.

In a second assay, on 8 animals (4 males and 4 females), the test substance at a dose of 400 mg/kg (i.e. 84.8 mg/kg in raw material) was dissolved in water and applied directly to the skin under a volume of 5 ml/kg.

Dose (mg/kg)				
21.2% solution	Active material	Volume (ml/kg)	number of animals	
			male	female
400	84.8	5	4	4
2000 (undilut.)	424	1.78	1	1

After 24 hours under a semi-occlusive dressing, no residual test substance was observed on removal of the dressing.
The animals given 400 mg/kg were checked for clinical signs, mortality and body weight gain for a period of 14 days following the single application of the test substance.

A necropsy was performed on each animal sacrificed during the study or sacrificed at the end of the study.

Result : 2000 mg/kg : tissular lesions on the whole depth of the skin were noted after removal of the dressing on day 2. The 2 treated animals were sacrificed on day 2 for humane reasons.

400 mg/kg: no cutaneous reactions and no deaths were noted.
Hypoactivity, tremors and reversible body weight loss between days 1 and 5 were noted in one female. No clinical signs and no alteration of the general behaviour were noted in the other animals.

Source : Atofina, Paris-la-Défense, France.

Test substance : The test article used as such was :
CH3SNa : 21.2% solution in water
Free NaOH : 1%

Conclusion : The LDo of SODIUM METHYLMER-CAPTIDE (21.2% in water), when administered by dermal route in rats was higher than or equal to 400 mg/kg (i.e. 84.8 mg/kg in raw material).

Reliability : (1) valid without restriction

Flag : Directive 67/548/EEC, Critical study for SIDS endpoint

13.08.2001 (7)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species : rabbit

Concentration : 21 % active substance

Exposure : Semiocclusive

Exposure time	:	3 minute(s)
Number of animals	:	6
Vehicle	:	
PDII	:	
Result	:	corrosive
Classification	:	highly corrosive (causes severe burns)
Method	:	OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year	:	1992
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : The potential irritant and/or corrosive effects of Sodium Methyl Mercaptide were evaluated on the skin of New Zealand White rabbits. Each of six rabbits received a 0.5 mL dose of the test article as a single dermal application. The dose was held in contact with the skin under a semi-occlusive binder for an exposure period of three minutes. Following the exposure periods, the gauze patch and/or binder were removed and the remaining test article was wiped from the skin using gauze moistened with deionized water. Test sites were evaluated for potential in-depth injury immediately following patch removal, one hour following patch removal and 24 hours following patch application.

Result : Exposure to the test article for a three-minute exposure period produced necrosis (grades 1-4) and blanching (grades 3-4) on 6/6 test sites by the one hour scoring interval. At the 24 hour scoring interval, necrosis (grades 1-2) was noted on 5/6 test sites and blanching (grades 2-4) and eschar (grades 1-3) were noted on 6/6 test sites.

Source	:	Atofina, Paris-la-Défense, France.
Test substance	:	Elf Atochem NA, sodium merthylmercaptide 21% in water.
Conclusion	:	The test substance is considered to be corrosive to the skin of the rabbit after a three-minute exposure period.
Reliability	:	(1) valid without restriction
Flag	:	Directive 67/548/EEC

13.08.2001 (8)

Species	:	rabbit
Concentration	:	21 % active substance
Exposure	:	Semiocclusive
Exposure time	:	1 hour(s)
Number of animals	:	1
Vehicle	:	
PDII	:	
Result	:	corrosive
Classification	:	corrosive (causes burns)
Method	:	OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year	:	1992
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : The potential irritant and/or corrosive effects of Sodium Methyl Mercaptide were evaluated on the skin of New Zealand White rabbits. One rabbit received a 0.5 mL dose of the test article as a single dermal application. The dose was held in contact with the skin under a semi-occlusive binder for an exposure period of one hour. Following the exposure periods, the gauze patch and/or binder were removed and the remaining test article was wiped from the skin using gauze moistened with deionized water. Test sites were evaluated for potential in-depth injury immediately following patch removal, one hour following patch removal and 24 hours following patch application.

Result : Exposure to the test article for a one-hour exposure period produced necrosis (grade 4) and moderate edema on the test sites by the one hour scoring interval. In addition, the outer most layer of skin appeared to be sloughing off and this animal exhibited increased activity and labored

breathing shortly after dosing. At the 24 hour scoring interval, eschar (grade 4) and severe edema were noted on the test site.

Source	:	Atofina, Paris-la-Défense, France.
Test substance	:	Elf Atochem NA, sodium merthylmercaptide 21% in water.
Conclusion	:	The test substance is considered to be corrosive to the skin of the rabbit after a one-hour exposure period.
Reliability	:	(1) valid without restriction
Flag	:	Directive 67/548/EEC

13.08.2001 (8)

Species	:	Rabbit
Concentration	:	19.9 % active substance
Exposure	:	Semiocclusive
Exposure time	:	4 hour(s)
Number of animals	:	1
Vehicle	:	
PDII	:	
Result	:	Corrosive
Classification	:	corrosive (causes burns)
Method	:	OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year	:	1981
GLP	:	Yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	A single dose of 0.5 ml of the test substance was prepared in its original form in a gauze patch then applied to 6 cm2 clipped area to 1 male New Zealand White rabbit. The test substance was held in contact with the skin for 4 hours by means of a semi-occlusive dressing. Residual test substance was removed by means of a dry dressing. The cutaneous reactions were observed 1 hour and 24 hours after removal of the dressing.
Result	:	One hour and 24 hours after the removal of the dressing, necrosis signs were observed at application site of the test substance. The animal was sacrificed after scoring at 24 hours. One hour and 24 hours after the removal of the dressing, necrosis signs were observed at application site of the test substance. The animal was sacrificed after scoring at 24 hours.
Source	:	Atofina, Paris-la-Défense, France.
Test substance	:	The test article used as such was : CH3SNa : 19.9% solution in water Na2S : 0.30% Free NaOH : 1.1% Releasable NaOH: 12.75%
Conclusion	:	The test substance was considered as corrosive when administered by cutaneous route in the Rabbit.
Reliability	:	(1) valid without restriction
Flag	:	Directive 67/548/EEC

13.08.2001 (9)

Species	:	rabbit
Concentration	:	19.6 % active substance
Exposure	:	Semiocclusive
Exposure time	:	4 hour(s)
Number of animals	:	1
Vehicle	:	
PDII	:	
Result	:	corrosive
Classification	:	corrosive (causes burns)
Method	:	OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year	:	1981
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	A single dose of 0.5 ml of the test substance was prepared in its original

form in a gauze patch then applied to 6 cm2 clipped area to 1 male New Zealand White rabbit. The test substance was held in contact with the skin for 4 hours by means of a semi-occlusive dressing. The cutaneous reactions were observed 1 hour and 24 hours after removal of the dressing. The test substance was not rinsed off after removal of the dressing. Residual test substance was removed by means of a dry dressing.

Result : One hour and 24 hours after the removal of the dressing, necrosis signs were observed at application site of the test substance.

Source : Atofina, Paris-la-Défense, France.

Test substance : The test article used as such was :
CH3SNa : 19.6% solution in methanol
Na2S : 1%
Free NaOH : =< 0.1%
Releasable NaOH: 12.2%

Conclusion : The test substance was considered as corrosive when administered by cutaneous route in the Rabbit.

Reliability : (1) valid without restriction

Flag : Directive 67/548/EEC

13.08.2001 (10)

5.2.2 EYE IRRITATION

5.3 SENSITIZATION

Type : Guinea pig maximization test

Species : guinea pig

Concentration : 1st: Induction 1 % active substance intracutaneous
2nd: Induction 1 % active substance occlusive epicutaneous
3rd: Challenge 10 % active substance occlusive epicutaneous

Number of animals : 30

Vehicle : physiol. saline

Result : not sensitizing

Classification : not sensitizing

Method : OECD Guide-line 406 "Skin Sensitization"

Year : 1981

GLP : yes

Test substance : as prescribed by 1.1 - 1.4

Method : Thirty guinea-pigs (15 males and 15 females) were allocated to 2 groups: a control group 1 (5 males and 5 females) and a treated group 2 (10 males and 10 females). The sensitization potential of the test substance was evaluated after a 10-day induction period during which time the animals were treated with the vehicle (control group) or the test substance (treated group). On day 1, in presence of Freund's complete adjuvant, 0.1 ml of the test substance at a concentration of 1 % in the vehicle was administered by intradermal route. On day 8, 0.5 ml of the test substance at a concentration of 1 % in the vehicle was applied by cutaneous route during 48 hours by means of an occlusive dressing. After a period of 12 days without treatment, a challenge cutaneous application of 0.5 ml of the vehicle (left flank) and 0.5 ml of the test substance at a concentration of 10% in the vehicle (right flank) were administered to all animals.
The test substance and the vehicle were prepared on a dry compress then applied to the skin and held in place for 24 hours by means of an occlusive dressing. Cutaneous reactions on the challenge application sites were then evaluated 24 and 48 hours after removal of the dressing.

After the final scoring period, the animals were sacrificed. No skin samples were taken from the challenge application sites from all the animals.

		The sensitivity of the guinea-pigs in C.I.T. experimental conditions were checked in a recent study with a positive sensitizer: Dinitro 2.4 Chlorobenzene. During induction period the test substance was applied at 0.05% (day 1) and 0.5% (day 8) concentrations. At cutaneous challenge application, 0.1% and 0.5% were tested on both flanks.
Result	:	No clinical signs and no deaths were noted. After 24 and 48 hours following removal of the dressing of the cutaneous challenge (test substance), no cutaneous reactions were recorded. The guinea pig showed a satisfactory sensitization response in 100 % using the positive sensitizer (DCNB).
Source	:	Atofina, Paris-la-Défense, France.
Test substance	:	21.2% sodium mercaptide solution in water (1% free NaOH).
Conclusion	:	According to the maximization method established by Magnusson and Kligman, no cutaneous reactions attributable to the sensitization potential of the test substance, SODIUM METHYLMERCAPTIDE, at the maximum non-irritant concentration of 10% were observed in guinea-pigs.
Reliability	:	(1) valid without restriction
Flag	:	Directive 67/548/EEC

13.08.2001 (11)

5.4 REPEATED DOSE TOXICITY

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Salmonella typhimurium reverse mutation assay
System of testing	:	Strains TA 1535, TA 1537, TA 102, TA 98, TA 100
Test concentration	:	312.5, 625, 1250, 2500 and 5000 µg/plate or 125, 250, 500, 1000 and 2000 µg/plate
Cycotoxic concentr.	:	Without S9: >= 1000 µg/plate With S9: >= 2500 µg/plate
Metabolic activation	:	with and without
Result	:	negative
Method	:	OECD Guide-line 471
Year	:	1983
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method :

The in vitro potential mutagenic activity of SODIUM METHYL MERCAPTIDE was investigated by the Ames test using 5 strains of bacteria Salmonella typhimurium: TA 1535, TA 1537, TA 102, TA 98 and TA 100. This test enables the detection of base-pair substitution and frameshift mutagens.

After a preliminary assay to define the concentrations to be used for the mutagenicity study, the test substance was tested on two independent assays. Each assay was carried out both in the absence and in the presence of a metabolic activation system, the S9 mix, prepared from a liver microsomal fraction S9 of rats treated with Aroclor 1254.
The methods used were:
- the direct plate incorporation method for the 2 assays without S9 mix and for the first assay with S9 mix,
- the preincubation method (1 h, 37 ° C) for the second assay with S9 mix.

The concentrations were:
312.5, 625, 1250, 2500 and 5000 µg/plate, except in the second test for the TA 98 and TA 102 strains without S9 mix:
1.25, 250, 500, 1000 and 2000 µg/plate, and for the TA 102 strain with S9 mix: 312.5, 625, 1250, 2500 and 4000 µg/plate.

The negative and solvent control results were equivalent to those usually obtained in the Laboratory. The number of revertants induced by the positive controls was higher than the spontaneous one, which demonstrated the sensitivity of this test and the efficacy of the S9 mix throughout this study.

Remark : The concentration above mentioned by the laboratory performing the study is related to the test article as such (sodium methyl mercaptan 31.4 % w/w). However, the toxicity, variable in strains, make impossible to use higher concentrations.

Result : The test substance SODIUM METHYL MERCAPTIDE did not induce any significant increase in the revertant number with or without S9 mix in any of the 5 strains.

Source : Atofina, Paris-la-Défense, France.

Test substance : 31.4% sodium mercaptide solution in water (0.06% free NaOH).

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

13.08.2001 (12)

Type : Chromosomal aberration test

System of testing : Human lymphocytes

Test concentration : 30, 60, 90, 120, 240, 480 µg/ml

Cycotoxic concentr. : Without S9: >= 240 µg/ml
With S9: >= 480 µg/ml

Metabolic activation : with and without

Result : Ambiguous

Method : OECD Guide-line 473

Year : 1983

GLP : Yes

Test substance : as prescribed by 1.1 - 1.4

Method : Sodium methylmercaptide was tested with or without a metabolic activation system, the S9 mix, prepared from a liver microsomal fraction (S9) of rats induced with Aroclor 1254.

For each culture, heparinised whole blood were added to culture medium containing a mitogen (phytohaemogglutinin) and incubated at 37°C.

After 48 hours, the conditions of treatment were as follows, using 2 cultures/experimental point:
. without S9 mix, the test or control substances remained in the culture medium either for 20 hours or for 44 hours, until harvest, i.e. approximately 1.5 times cell cycle or 24 hours after.
. with S9 mix, the test or control substances remained in the culture medium for 3 hours. The cells were then rinsed and fresh culture medium was added. The cultures were then incubated either for 20 hours or for 44 hours, after the beginning of treatment until harvest, i.e. approximately 1.5 times cell cycle and 24 hours after.

Each culture was then treated for 1.5 hours with a colcemid solution to block them at the metaphase-stage of mitosis and harvested. The chromosomal preparations were stained and screened microscopically for mitotic index and for aberrations: 200 well-spread metaphases per dose were read, whenever possible.

After preliminary test, the cells were exposed to the following doses expressed as active material: 480, 240, 120, 90, 60 and 30 µg/ml. The top dose for scoring was selected according to the criteria specified in the international regulations. Since the test substance was toxic, the top dose was based on the level of toxicity: a toxic dose giving a reduction higher than 50% of mitotic index.

Therefore, chromosome aberrations were scored on the slides corresponding to the following doses:
without S9 mix
. 30, 60, 120, 240 µg/ml, lst harvest
. 30, 60, 90, 120 µg/ml, 2nd harvest.
with S9 mix
. 30, 60, 120, 240, 480 µg/ml, lst harvest
. 30, 60, 120 µg/ml, 2nd harvest.

Remark : The concentration above mentioned by the laboratory performing the study is related to the active material.

Result : Sodium methylmercaptide did not induce structural chromosome aberrations both with and without S9 mix for both harvests. However, without S9 mix an increase in the number of polyploid cells was recorded at the 44-hour harvest at 90 and 120 µg/ml (4.0% and 14.5% respectively vs. 0%). Therefore, a complementary test without S9 mix at the 44-pour harvest was performed using the following doses: 50, 100 and 150 µg/ml. Since the mitotic index was reduced by more than 90% at 150 µg/ml, only slides from the 50 and 100 µg/ml treatment-level were scored. 3% polyploidy was noted at 100 µg/ml and 0% at 50 µg/ml.

The frequencies of cells with structural chromosome aberrations of the vehicle and positive controls were as specified in acceptance criteria and within the range of the historical data for both tests and both harvest times.

	Without S9			With S9		
	%cells with chromosomal aberrations		%cells with numerical aberrations	%cells with chromosomal aberrations		%cells with numerical aberrations
Dose (µg/ml)	+gap	-gap		+gap	-gap	
	Hours of treatment/harvest time					
	20 hours/20 hours			3 hours/20 hours		
0	2.0	1.5	0	1.0	0.5	1.0
30	1.5	0.5	1.0	1.5	1.0	1.0
60	0.5	0.5	0	1.0	1.0	1.0
120	2.0	2.0	0.5	1.5	0.5	0.5
240	1.8	0.9	0.9	1.5	1.0	0
480				1.7	0.6	1.2
+ control	35.0	31.5	0	40.0	34.5	0
	44 hours/44 hours			3 hours/44 hours		
0	1.5	1.5	0	0.5	0.5	0
30	1.0	1.0	0.5	0	0	0
60	0.5	0	0	1.5	1.0	0
90	2.0	1.5	4.0			
120	0	0	14.5	0	0	1.0
	44 hours/44 hours					
0	0.5	0	0			
50	0	0	0			
100	0	0	3.0			

Source : Atofina, Paris-la-Défense, France.
Test substance : 21.21% sodium mercaptide solution in water (0.93% free NaOH).
Conclusion : SODIUM METHYLMERCAPTIDE did not induce structural chromosome aberrations but could induce numerical aberrations (polyploidy) in cultured human lymphocytes.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint

13.08.2001 (13)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Micronucleus assay
Species	:	mouse
Sex	:	male/female
Strain	:	other: OF1
Route of admin.	:	gavage
Exposure period	:	Two oral treatment at 24-hour interval
Doses	:	0, 12.5, 25 and 50 mg/kg/d
Result	:	negative
Method	:	OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year	:	1997
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : A preliminary toxicity test was performed to define the dose-levels to be used for the cytogenetic study. In the main study, three groups of five male and five female Swiss Ico: OF1 (IOPS Caw) mice received two oral treatments of SODIUM METHYLMERCAPTIDE at dose-levels of 12.5, 25 or 50 mg/kg/day, at a 24-hour interval.
One group of five males and five females received the vehicle (distilled water) under the same experimental conditions, and acted as control group. One group of five males and five females received the positive control test substance (cyclophosphamide) once by oral route at the dose-level of 50 mg/kg. The animals of the treated and vehicle control groups were killed 24 hours after the last treatment and the animals of the positive control group were killed 24 hours after the single treatment. Bone marrow smears were then prepared. For each animal, the number of the micronucleated polychromatic erythrocytes (MPE) was counted in 2000 polychromatic erythrocytes. The polychromatic (PE) and normochromatic (NE) erythrocyte ratio was established by scoring a total of 1000 erythrocytes (PE+NE).

Result : All the dose-levels were expressed in terms of active material taking into account a 32.8% active material content in the supplied test substance.

PRELIMINARY TOXICITY TEST
In order to select the top dose-level for the cytogenetic study, 500, 100, and 50 mg/kg/day were tested. At 500 mg/kg/day, all the treated animals (three males and three females) died 2 minutes following the first treatment. At 100 mg/kg/day, the three treated males showed sedation, lateral recumbency and dyspnea 2 minutes following the first treatment. Two minutes later, 1/3 males was found dead and sedation was noted in the surviving animals. No second treatment was performed at this dose-level. At 50 mg/kg/day, 1/3 males was found dead 24 hours after the second treatment, and reddish discharge was noted in the mouth area of this animal. No clinical signs and no mortality related to the test substance were noted in females at this dose-level.
The top dose-level for the cytogenetic test was selected according to the criteria specified in the international guidelines; since toxic effects were noted, the top dose-level was based on the toxicity level, such that a higher dose-level was expected to induce lethality. Consequently, 50 mg/kg/day was selected as the top dose-level. The two other dose-levels were 25 and 12.5 mg/kg/day.

CYTOGENETIC TEST
No clinical signs and no mortality were observed in the animals of both sexes given 12.5, 25 or 50 mg/kg/day. For both males and females, the mean values of MPE as well as the PE/NE ratio in the groups treated with

the test substance, were equivalent to those of the vehicle group and no significant difference was noted. The mean values of MPE as well as the PE/NE ratio for the vehicle and positive controls were consistent with our historical data.
Cyclophosphamide induced a highly significant increase ($p<0.001$) in the frequency of MPE, indicating the sensitivity of the test system. The study was therefore considered valid.

Source : Atofina, Paris-la-Défense, France.
Test substance : 32.8% sodium mercaptide solution in water (0.5% free NaOH).
Conclusion : SODIUM METHYLMERCAPTIDE does not induce damage to the chromosomes or the mitotic apparatus of mice bone marrow cells after two oral administrations, at a 24-hour interval, at the dose-levels of 12.5, 25 or 50 mg/kg/day.
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
13.08.2001 (14)

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

5.11 ADDITIONAL REMARKS

(1) Data from laboratory tests Atofina Netherlands

(2) KowWin (LogKow) Log P Calculation

(3) Elf Atochem SA. Sodium methyl mercaptide. Détermination de la biodégradabilité facile. Essai en fiole fermées. Centre d'Application de Levallois, référence 95/SAEk/1243/PB, 14/11/95.

(4) Elf Atochem S.A.(2000); "Methyl Mercaptan 33% sodium: Acute toxicity to daphnias" Centre d'Application de Levallois study no.604/99/A

(5) ELF ATOCHEM (1989) Acute oral toxicity in rats. CIT report no. 5161 TAR, 1st August 1989.

(6) ELF ATOCHEM (1989) Acute oral toxicity in rats. CIT Report no. 5167 TAR, 30 August 1989.

(7) ELF ATOCHEM (1994) Acute dermal toxicity in rats. CIT Report no. 10874, 14 January 1994.

(8) ELF ATOCHEM (1997) A dermal irritation/corrosivity study in rabbits with sodium methyl mercaptide. Springborn report no. 3255.110, 2nd May 1997.

(9) ELF ATOCHEM (1989) Methyl mercaptide de sodium, solution aqueuse à 18%. Evaluation de l'irritation cutanée chez le lapin. CIT Report no. 5163 TAL, 10 July 1989.

(10) ELF ATOCHEM (1989) Methyl mercaptide de sodium, solution methanolique à 18%. Evaluation de l'irritation cutanée chez le lapin. CIT Report no. 5169 TAL, 4 July 1989.

(11) ELF ATOCHEM (1994) Skin sensitization test in guinea pig with methyl mercaptide. CIT report no. 10875 TSG, January 1994.

(12) ELF ATOCHEM (1992) Sodium methyl mercaptide. Reverse mutation assay by the Ames test. CIT Report no. 9102 MMO, 7 August 1992.

(13) ELF ATOCHEM (1995) In vitro mamalian chromosome aberration test in cultured human lymphocytes with sodium methylmercaptide. CIT report no. 12086 MLH, 15 November 1995.

(14) ELF ATOCHEM (1999) Bone marrow micronucleus test by oral route in mice with sodium methylmercaptide. CIT report no.18114 MAS, 27 July 1999.

I U C L I D

Data Set

Existing Chemical	:	ID: 7783-06-4
CAS No.	:	7783-06-4
EINECS Name	:	hydrogen sulphide
EINECS No.	:	231-977-3
TSCA Name	:	Hydrogen sulfide (H2S)
Molecular Formula	:	H2S

Producer Related Part

Company	:	ATOFINA Chemicals Inc.
Creation date	:	06.11.2001

Substance Related Part

Company	:	ATOFINA Chemicals Inc.
Creation date	:	06.11.2001
Memo	:	
Printing date	:	13.11.2001
Revision date	:	
Date of last Update	:	13.11.2001
Number of Pages	:	8
Chapter (profile)	:	Chapter: 5
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

5.1.1 ACUTE ORAL TOXICITY

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	5
Vehicle	:	
Exposure time	:	4 hour(s)
Value	:	= 675 ppm
Method	:	
Year	:	
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Animals exposed for 4 hours to hydrogen sulfide or air and observed for 14 days and examined for gross pathology, such as general or local hemorrhage and adhesions. Mortality and visually apparent behavior such as exploring, huddling, preening, and obvious distress were noted during the 4 hr exposure. The rats were deprived of food and water during exposure.
Result	:	Dose Mortality ppm sham 0/10 400 3/10 440 3/10 475 7/10 500 8/10 525 8/10 554 9/10 600 10/10 LC50 444 (416-473 ppm) Animals which survived the first 24 hours after exposure survived to the end of the 14 day oberservation period.
Test condition	:	Hydrogen sulfide supplied by Union Carbide Corp
Conclusion	:	LC50 = 444 ppm (416-473 ppm)
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

12.11.2001 (5)

5.1.3 ACUTE DERMAL TOXICITY

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

5.2.2 EYE IRRITATION

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	inhalation
Exposure period	:	6hrs/day
Frequency of treatment	:	5 days/wk for 90 days
Post obs. period	:	10 days following last exposure
Doses	:	0, 10.1, 30.5, or 80.0 ppm
Control group	:	yes, concurrent no treatment
NOAEL	:	= 80 ppm
Method	:	OECD Guide-line 413 "Subchronic Inhalation Toxicity: 90-day Study"
Year	:	1981
GLP	:	yes
Test substance	:	other TS
Method	:	A 90-day inhalation toxicity study using Fisher 344 rats, Sprague Dawley rats, and B6C3F1 mice (exposed simulateously int he same chamber) were conducted with H2S vapor. Three grps (15 male/15 female per grp) were designated as T-1, T-II, and T-III and exposed to atmospheres of 10.1, 30.5, and 80.0 ppm, respectively. In addition, control grps (15 male/15 female) were exposed to clean air only and were hanndles in a similar manner to that of the test animals. The duration of exposure was 6hrs/day, 5days/wk, for at least 90 days.
Result	:	No mortality was observed during the 90d study. Clinical observations included crustiness associated with the animal's ear tag, crusty nose, crusty muzzle, lacrimation, rales, yellow/brown stained fur and red stained fur. A significant decrease in body weight gain was observe in all treatment grps after the first week of exposure. Body weights of the treated grps continued to lag behindweights of the control grp over the next 12 weeks. No significant effects were noted in food consumption, opthamology, neurological function, clinical pathology, or organ weights. Gross and histological studies on "principle" animals did not reveal any lesions that were attributable to test article exposure. Lesions present were of a spontaneous nature and were of the type and severity normally expected with Fischer rats this age. Special neuropathologic studies performed on teased fibers from muscular and sural branches of the tibial nerve, together with Epon embedded specimens from these nerves and specimens from cervical and lumber spinal cord from untreated controls and the high dose grp (T-III), did not show neuropathologic changes.
Source	:	Chevron Phillips Chemical Company, LP
Test substance	:	H2S Cas # 7783-06-4
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

13.11.2001 (2)

Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	90 days
Frequency of treatment	:	6hrs/day, 5 days/week

Post obs. period	:	10 days after last exposure
Doses	:	10.1, 30.5, and 80.0 ppm
Control group	:	yes, concurrent no treatment
NOAEL	:	= 30 - 80 ppm
Method	:	OECD Guide-line 413 "Subchronic Inhalation Toxicity: 90-day Study"
Year	:	1981
GLP	:	yes
Test substance	:	other TS
Method	:	A 90-day inhalation toxicity study using Fisher 344 rats, Sprague Dawley rats, and B6C3F1 mice (exposed simulateously int he same chamber) were conducted with H2S vapor. Three grps (15 male/15 female per grp) were designated as T-1, T-II, and T-III and exposed to atmospheres of 10.1, 30.5, and 80.0 ppm, respectively. In addition, control grps (15 male/15 female) were exposed to clean air only and were hanndles in a similar manner to that of the test animals. The duration of exposure was 6hrs/day, 5days/wk, for at least 90 days.
Result	:	NOAEL females - 30 ppm males - 80 ppm There was no mortality during the 90 day study. Clinical observations included crustiness associated with the animal's ear tag, crusty nose, eyes and muzzel, lacrimation, rales, yellow/brown stained fur and red stained fur. A significant decrease in body weight gains of all treatment groups of both sexes was noted after the first week of exposure. Body weights of the treated groups continued to lag behind the control group over the next 12 weeks. No significant were noted with respect to food consumption, opthalmology, nuerological function, clinical pathology, and organ weight data. Gross and histopathologic studies did not reveal any lesions attributable to test article exposure. Special neuropathological studies preformed on teased fibers from muscular and sural branches of the tibial nerve, together with Epon embedded specimens from cervical and lumber spinal cord from control and high dose animals did not show neuropathologic changes.
Source	:	Chevron Phillips Chemical Company, LP
Test substance	:	H2S Cas # 7783-06-4
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

13.11.2001 (3)

Species	:	mouse
Sex	:	male/female
Strain	:	B6C3F1
Route of admin.	:	inhalation
Exposure period	:	90 days
Frequency of treatment	:	6 hrs/day, 5 days/wk
Post obs. period	:	10 days after last exposure
Doses	:	10.1, 30.5, or 80.0 ppm
Control group	:	yes, concurrent no treatment
NOAEL	:	= 30 ppm
Method	:	OECD Guide-line 413 "Subchronic Inhalation Toxicity: 90-day Study"
Year	:	1981
GLP	:	yes
Test substance	:	other TS
Method	:	A 90-day inhalation toxicity study using Fisher 344 rats, Sprague Dawley rats, and B6C3F1 mice (exposed simulateously int he same chamber) were conducted with H2S vapor.

		Three grps (15 male/15 female per grp) were designated as T-1, T-II, and T-III and exposed to atmospheres of 10.1, 30.5, and 80.0 ppm, respectively. In addition, control grps (15 male/15 female) were exposed to clean air only and were hanndles in a similar manner to that of the test animals. The duration of exposure was 6hrs/day, 5days/wk, for at least 90 days.
Result	:	No mortality was observed during the 90d study. Clinical observations included crustiness associated with the animal's ear tag, crusty nose, crusty muzzle, lacrimation, rales, yellow/brown stained fur and red stained fur. A significant decrease in body weight gain was observe in all treatment grps after the first week of exposure. Body weights of the treated grps continued to lag behindweights of the control grp over the next 12 weeks. No significant effects were noted in food consumption, opthamology, neurological function, clinical pathology, or organ weights. Gross and histological studies on "principle" animals did not reveal any lesions that were attributable to test article exposure. Lesions present were of a spontaneous nature and were of the type and severity normally expected with Fischer rats this age. Special neuropathologic studies performed on teased fibers from muscular and sural branches of the tibial nerve, together with Epon embedded specimens from these nerves and specimens from cervical and lumber spinal cord from untreated controls and the high dose grp (T-III), did not show neuropathologic changes.
Source	:	Chevron Phillips Chemical Company, LP
Test substance	:	H2S Cas # 7783-06-4
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

13.11.2001 (1)

5.5 GENETIC TOXICITY 'IN VITRO'

5.6 GENETIC TOXICITY 'IN VITRO'

5.7 CARCINOGENITY

5.8 TOXICITY TO REPRODUCTION

Type	:	other: OECD 421
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	6 hour/day
Frequency of treatment	:	7 days/week
Premating exposure period		
Male	:	2 weeks
Female	:	2 weeks
Duration of test	:	2 weeks prior to breeding, 2 wk mating period. Females - gestation day 0-19, postnatal days 5-18. Males exposed for 70 consecutive days
Doses	:	0, 10, 30, 80 ppm
Control group	:	yes, concurrent no treatment
NOAEL Parental	:	= 80 ppm

NOAEL F1 Offspr.	:	= 80 ppm
Method	:	other: OECD 421
Year	:	1995
GLP	:	yes
Test substance	:	other TS
Method	:	This study investigated the effects of perinatal exposure by inhalation to hydrogen sulfide (H2S) on pregnancy outcomes, offspring prenatal and postnatal development, or offspring behavior. Virgin male and female Sprague-Dawley rats (12 rats/sex/concentration) were exposed (0, 10, 30, or 80 ppm H2S; 6h/day, 7 days/week) for 2 weeks prior to breeding. Exposures continued during a 2-week mating period (evidence of copulation = GD 0 = GD 0) and then from GD 0 through GD 19. Exposure of dams and their pups (eight rats/litter after culling) resumed between PND 5 and 18. Adult male rats were exposed for 70 consecutive days. Offspring were evaluated using motor activity (PND 13, 17, 21, and 60 ± 2), passive avoidance (PND 22 ± 1 and 62 ± 3), functional observation battery (PND 60 ± 2), acoustic startle response (PND 21 and 62 ± 3), and neuropathology (PND 23 ± 2 and 61 ± 2).
Result	:	There were no deaths and no adverse physical signs observed in F0 male or female rats during the study. A statistically significant decrease in feed consumption was observed in F0 male rats from the 80 ppm H2S exposure group during the first week of exposure. There were no statistically significant effects on the reproductive performance of the F0 rats as assessed by the number of females with live pups, litter size, average length of gestation, and the average number of implants per pregnant female. Exposure to H2S did not affect pup growth, development, or performance on any of the behavioral tests.
Source	:	Chevron Phillips Chemical Company, LP
Test substance	:	Hydrogen sulfide supplied by Holox gases (Cary, NC)
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

13.11.2001 (4)

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	6 hours/day
Frequency of treatment	:	7days/wk
Duration of test	:	2 weeks prior to breeding, during 2-week mating period, then from gestation day 0-19. No exposures occurred through the remainder of gestation and during the period of parturition (gestation day (GD) 20 through postnatal day (PND) 4). sing
Doses	:	0, 10, 30, or 80 ppm
Control group	:	yes, concurrent no treatment
NOAEL Maternalt.	:	> 80 ppm
NOAEL Teratogen	:	> 80 ppm
Method	:	other: OECD 421
Year	:	1995
GLP	:	yes
Test substance	:	other TS
Method	:	This study investigated the effects of perinatal exposure by inhalation to hydrogen sulfide (H2S) on pregnancy outcomes, offspring prenatal and postnatal development, or offspring behavior. Virgin male and female Sprague-Dawley rats (12 rats/sex/concentration) were exposed (0, 10, 30, or 80 ppm H2S; 6h/day, 7 days/week) for 2 weeks prior to breeding. Exposures continued during a 2-week mating period (evidence of

copulation = GD 0 = GD 0) and then from GD 0 through GD 19. Exposure of dams and their pups (eight rats/litter after culling) resumed between PND 5 and 18. Adult male rats were exposed for 70 consecutive days. Offspring were evaluated using motor activity (PND 13, 17, 21, and 60 ± 2), passive avoidance (PND 22 ± 1 and 62 ± 3), functional observation battery (PND 60 ± 2), acoustic startle response (PND 21 and 62 ± 3), and neuropathology (PND 23 ± 2 and 61 ± 2).

Result : There were no deaths and no adverse physical signs observed in F0 male or female rats during the study. A statistically significant decrease in feed consumption was observed in F0 male rats from the 80 ppm H2S exposure group during the first week of exposure. There were no statistically significant effects on the reproductive performance of the F0 rats as assessed by the number of females with live pups, litter size, average length of gestation, and the average number of implants per pregnant female. Exposure to H2S did not affect pup growth, development, or performance on any of the behavioral tests.

Source : Chevron Phillips Chemical Company, LP

Test substance : Hydrogen sulfide supplied by Holox gases (Cary, NC)

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

13.11.2001 (4)

5.10 OTHER RELEVANT INFORMATION

5.11 EXPERIENCE WITH HUMAN EXPOSURE

(1) CIIT. Toxigenics, Inc. 90-day vapor inhalation toxicity study of hydrogen sulfide in B6C3F1 mice. CIIT Docket No 22063. Chemical Industry Institute of Toxicology, Research Triangle Park, NC. 1983

(2) CIIT. Toxigenics, Inc. 90-day vapor inhalation toxicity study of hydrogen sulfide in Fischer 344 rats. CIIT Docket No 22063. Chemical Industry Institute of Toxicology, Research Triangle Park, NC. 1983

(3) CIIT. Toxigenics, Inc. 90-day vapor inhalation toxicity study of hydrogen sulfide in Sprague-Dawley rats. CIIT Docket No 22063. Chemical Industry Institute of Toxicology, Research Triangle Park, NC. 1983

(4) Dorman, DC et al. 2000. Fertility and developmental neurotoxicity effects of inhaled hydrogen sulfide in Sprague-Dawley rats. Neurotoxicology and Teratology. 22:71-84.

(5) Tansy M.F., et al. 1981. Acute and subchronic toxicity studies of rats exposed to vapors of methyl mercaptan and other reduced-sulfur compounds. J. Tox. Env. Health. 8:71-88.